SPECTRUM PHARMACEUTICALS INC
Form 10-K
March 14, 2017
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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

Form 10-K

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x ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2016

¨ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

Commission File Number: 001-35006

SPECTRUM PHARMACEUTICALS, INC.
(Exact Name of Registrant as Specified in its Charter)

Delaware	93-0979187
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

11500 South Eastern Avenue, Suite 240
Henderson, Nevada 89052
(Address of principal executive offices)
(702) 835-6300
(Registrant's telephone number, including area code)
Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	Name of Each Exchange on Which Registered
Common Stock, $0.001 par value	The NASDAQ Stock Market, LLC
Rights to Purchase Series B Junior Participating Preferred Stock	

Securities registered pursuant to Section 12(g) of the Act:
None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ¨ No x
Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ¨ No x
Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes x No ¨

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes x No ¨

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K x

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer ¨	Accelerated filer x
Non-accelerated filer ¨ (Do not check if a smaller reporting company)	Smaller reporting company ¨

Indicate by check mark whether the Registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ¨ No x

As of June 30, 2016, the aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant was $424,190,348 (based upon the $6.57 per share closing sale price for shares of the Registrant's Common Stock as reported by the NASDAQ Global Select Market on June 30, 2016, the last trading date of the Registrant's most recently completed second fiscal quarter).

As of February 28, 2017, approximately 80,252,585 shares of the Registrant's Common Stock, $0.001 par value, were outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's Proxy Statement for the registrant's 2017 Annual Meeting of Stockholders, to be filed on or before May 1, 2017 are incorporated by reference into Part III, Items 10-14 of this Annual Report on Form 10-K.

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Cautionary Note Concerning Forward-Looking Statements

This Annual Report on Form 10-K contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934 as amended, or the Exchange Act, in reliance upon the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Forward-looking statements include, without limitation, statements regarding our future product development activities and costs, the revenue potential (licensing, royalty and sales) of our products and product candidates, the success, safety and efficacy of our drug products, revenues and revenue assumptions, clinical studies, including designs and implementation, development timelines, product acquisitions, litigation and regulatory actions, liquidity and capital resources and trends, and other statements containing forward-looking words, such as, “believes,” “may,” “could,” “will,” “expects,” “intends,” “estimates,” “anticipates,” “plans,” “seeks,” “continues,” or the negative thereof o thereon or similar terminology (although not all forward-looking statements contain these words). Such forward-looking statements are based on the reasonable beliefs of our management as well as assumptions made by and information currently available to our management. Readers should not put undue reliance on these forward-looking statements. Forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified; therefore, our actual results may differ materially from those described in any forward-looking statements. Factors that might cause such a difference include, but are not limited to, those discussed elsewhere in this Annual Report on Form 10-K, and the following factors:

- our ability to successfully develop, obtain regulatory approval for and market our products;
- our ability to continue to grow sales revenue of our marketed products;
- risks associated with doing business internationally;
- our ability to generate and maintain sufficient cash resources to fund our business;
- our ability to enter into strategic alliances with partners for manufacturing, development and commercialization;
- efforts of our development partners;
- the ability of our manufacturing partners to meet our timelines;
- the ability to timely deliver product supplies to our customers;
- our ability to identify new product candidates and to successfully integrate those product candidates into our operations;
- the timing and/or results of pending or future clinical trials, and our reliance on contract research organizations;
- our ability to protect our intellectual property rights;
- competition in the marketplace for our drugs;
- delay in approval of our products or new indications for our products by the U.S. Food and Drug Administration, or the FDA;
- actions by the FDA and other regulatory agencies, including international agencies;
- securing positive reimbursement for our products;
- the impact of any product liability, or other litigation to which we are, or may become a party;
- the impact of legislative or regulatory reform of the healthcare industry and the impact of recently enacted healthcare reform legislation;
- the availability and price of acceptable raw materials and components from third-party suppliers, and their ability to meet our demands;
- our ability, and that of our suppliers, development partners, and manufacturing partners, to comply with laws, regulations and standards, and the application and interpretation of those laws, regulations and standards, that govern or affect the pharmaceutical and biotechnology industries, the non-compliance with which may delay or prevent the development, manufacturing, regulatory approvals and sale of our products;
- defending against claims relating to improper handling, storage or disposal of hazardous chemical, radioactive or biological materials which could be time consuming and expensive;

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- our ability to maintain the services of our key executives and technical and sales and marketing personnel;
- the difficulty in predicting the timing or outcome of product development efforts and regulatory approvals; and
- demand and market acceptance for our approved products.

All subsequent written and oral forward-looking statements attributable to us or by persons acting on our behalf are expressly qualified in their entirety by these cautionary statements.

In addition, past financial or operating performance is not necessarily a reliable indicator of future performance, and you should not use our historical performance to anticipate results or future period trends. We can give no assurances that any of the events anticipated by the forward-looking statements will occur or, if any of them do, what impact they will have on our results of operations and financial condition. Except as required by law, we do not undertake to update any such forward-looking statements and expressly disclaim any duty to update the information contained in this Annual Report on Form 10-K.

Unless the context otherwise requires, all references in this Annual Report on Form 10-K to the “Company”, “we,” “us,” “our,’ “Spectrum” and “Spectrum Pharmaceuticals” refer to Spectrum Pharmaceuticals, Inc. and its subsidiaries and other consolidated entities, as a consolidated entity. We primarily conduct our business activities as Spectrum Pharmaceuticals.

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PART I

ITEM 1. BUSINESS

Company Overview

Spectrum Pharmaceuticals, Inc. is a biotechnology company, with a primary strategy comprised of acquiring, developing, and commercializing a broad and diverse pipeline of late-stage clinical and commercial products. We have an in-house clinical development organization with regulatory and data management capabilities, a commercial infrastructure, and a field sales force for our marketed products. Currently, we have six approved oncology/hematology products that target different types of cancer including: non-Hodgkin's lymphoma, or NHL, advanced metastatic colorectal cancer, or mCRC, acute lymphoblastic leukemia, or ALL, and multiple myeloma, or MM.

We also have three drugs in mid-to-late stage development (defined as Phase 2 and Phase 3):

- ROLONTIS (previously referred to as SPI-2012 or LAPS-G-CSF) for chemotherapy-induced neutropenia.
- QAPZOLA (previously referred to as APAZIQUONE) for immediate intravesical instillation in post-transurethral resection of bladder tumors in patients with non-muscle invasive bladder cancer, or NMIBC.
- POZIOTINIB, a novel pan-HER inhibitor used in the treatment of patients with a variety of solid tumors, including breast and lung cancer.

Our passion to identify, develop, and deliver important options for patients suffering from cancer is behind every action we take. We are committed to excellence, and strive to make a difference in the lives of cancer patients every day.

Cancer Background and Market Size

Cancer is a group of diseases characterized by the uncontrolled growth and spread of abnormal cells, which can result in death. The development of cancer is multi-factorial and includes both external factors (tobacco, infectious organisms, chemicals, and radiation) and internal factors (inherited mutations, hormones, immune conditions, and mutations that occur from exposure to environmental factors or errors in making DNA (deoxyribonucleic acid) during normal cell division). These causal factors may act together or in sequence to initiate or promote the development of cancer. Ten or more years often pass between exposure to these factors and the development of detectable cancer. Cancer is treated through surgery, radiation, chemotherapy, hormone therapy, immune therapy, and/or targeted drug

therapy.

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According to the American Cancer Society's publication Cancer Facts & Figures 2016, cancer is the second leading cause of death in the U.S. (only behind heart disease). In the U.S., approximately 1.7 million new cancer cases were expected to be diagnosed in 2016 and over 596,000 persons were expected to die from the disease. Anyone can develop cancer. Since the risk of being diagnosed with cancer increases with age, most cases occur in adults who are middle aged or older. About 77% of all cancers are diagnosed in people 55 years of age and older. In the U.S., men have slightly less than a 1 in 2 lifetime risk of developing cancer; for women, the risk is a little more than 1 in 3. These probabilities are estimated based on the overall experience of the general population. Individuals within the population may have higher or lower risk because of differences in exposures (e.g., smoking), and/or genetic susceptibility. In addition, currently available treatments are variably effective in the different cancers and individual patients. Together these patients' risks and the treatment limitations suggest a significant current and long-term demand for improved and novel cancer treatments.

Product Portfolio

We have a product portfolio consisting of both commercial stage and development stage products that address various cancer types (see the section titled Research and Development below for our pipeline of cancer therapeutics that are in various development stages). Our commercialized products and products in development may have serious adverse effects, or SAEs, that could result in a negative impact on sales and delays, or removal of regulatory approval. For further information on these SAEs, see the risk factor within accompanying Item 1A. Risk Factors – Risks Related to Our Business --Reports of adverse events or safety concerns involving each of our products or similar agents, sold by us or our development partners and/or licensees, could delay or prevent us from obtaining or maintaining regulatory approval or negatively impact sales.

We remain committed to growing the sales of our currently marketed products, as we strive to maintain a robust development pipeline to deliver important options for patients suffering from cancer, as discussed below.

Commercialized Products

FUSILEV

FUSILEV (levoleucovorin) is a novel folate analog and the pharmacologically active isomer (the levo-isomer) of the racemic compound, calcium leucovorin. Leucovorin is a mixture of equal part of both isomers: the pharmacologically active levo-isomer and the inactive dextro-isomer. Preclinical studies have demonstrated that the inactive dextro-isomer may compete with the active levo-isomer for uptake at the cellular level. By removing the inactive dextro form, the dosage of FUSILEV is one-half that of leucovorin and patients are spared the administration of an inactive substance. FUSILEV is approved as a ready-to-use solution, and as freeze-dried powder. FUSILEV has the following indications for use:

- in combination chemotherapy with 5-fluorouracil in the palliative treatment of patients with advanced mCRC;
- for rescue after high-dose methotrexate, or MTX, therapy in osteosarcoma; and
- to diminish the toxicity and counteract the effects of impaired MTX elimination and of inadvertent over dosage of folic acid antagonists.

FOLOTYN

FOLOTYN (pralatrexate injection), a folate analogue metabolic inhibitor, was discovered by Memorial Sloan-Kettering Cancer Center, SRI International and Southern Research Institute and developed by Allos Therapeutics, Inc., or Allos. In September 2009, the FDA granted accelerated approval for FOLOTYN for use as a single agent for the treatment of patients with relapsed or refractory peripheral T-cell lymphoma, or PTCL. FOLOTYN was the first chemotherapy approved by the FDA, under its accelerated approval program, for the treatment of relapsed or refractory PTCL and has been available to patients in the U.S. since October 2009. According to the Lymphoma Research Foundation, lymphoma is the most common blood cancer. Hodgkin's lymphoma and NHL are the two main forms of lymphoma. Lymphoma occurs when lymphocytes, a type of white blood cell, grow abnormally and accumulate in one or more lymph nodes or lymphoid tissues. The body has two main types of lymphocytes that can develop into lymphomas: B-lymphocytes, or B-cells, and T-lymphocytes, or T-cells.

PTCL comprises a group of rare and aggressive NHLs that develop from mature T-cells and accounts for approximately 5 to 15% of all NHL cases in the U.S. and Europe.

Based on preclinical studies, we believe that FOLOTYN selectively enters cells expressing reduced folate carrier, or RFC-1, a protein that is frequently over expressed on cancer cells compared to normal cells. Once inside cancer cells,

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FOLOTYN is efficiently polyglutamylated and retained inside the cells for a longer time. FOLOTYN and its polyglutamates inhibit dihydrofolate reductase, or DHFR, an enzyme critical in the folate pathway, thereby interfering with DNA and RNA synthesis and triggering cancer cell death.

The safety and efficacy of FOLOTYN was evaluated in an open-label, single-arm, multi-center, international trial that enrolled patients with relapsed or refractory PTCL. One hundred and eleven patients were treated with FOLOTYN at 30 mg/m2 once weekly by IV push over three to five minutes for six weeks in seven-week cycles until disease progression or unacceptable toxicity. Of the 111 patients treated, 109 patients were evaluable for efficacy. The primary efficacy endpoint was overall response rate (complete response, complete response unconfirmed, and partial response) as assessed by International Workshop Criteria, or IWC. Of the 109 evaluable patients, 27% of patients achieved a response that met these criteria.

In addition to its approved indication, FOLOTYN is being investigated in a Phase 1 study in combination with the CHOP chemotherapy regimen. Once the proper dose of FOLOTYN in combination with CHOP has been determined, we expect to plan a Phase 3 study of the combinations of FOLOTYN and CHOP, and BELEODAQ and CHOP, compared to CHOP alone for the treatment of first line PTCL. The Phase 1 study and the Phase 3 study concept are also the current post-marketing requirements for the FDA's accelerated approval of our currently marketed indication for FOLOTYN.

ZEVALIN

ZEVALIN (ibritumomab tiuxetan) injection for intravenous use is a prescription medication that is part of a three step treatment regimen consisting of: two treatments of rituximab and one treatment of Yttrium-90 (Y-90) ZEVALIN. The National Cancer Institute, or NCI, estimated 73,000 new cases of NHL in the U.S. in 2016. Rituximab is used to reduce the number of B-cells in the blood and Y-90 ZEVALIN is then given to treat NHL. It is currently approved in the U.S. and more than 40 countries outside the U.S. including countries in Europe, Latin America and Asia for (i) treatment of patients with recurring, low-grade or follicular B-cell NHL after other anticancer drugs are no longer working, and (ii) newly diagnosed follicular NHL following a response to initial anticancer therapy.

MARQIBO

MARQIBO is a novel, sphingomyelin/cholesterol liposome-encapsulated formulation of the FDA-approved anticancer drug vincristine. MARQIBO's approved indication is for the treatment of adult patients with ALL in second or greater relapse or whose disease has progressed following two or more lines of anti-leukemia therapy. In the U.S., approximately 6,000 patients per year are diagnosed with ALL, of which approximately 1,600 can be categorized as ALL in second or greater relapse.

MARQIBO was studied in an international, open-label, multi-center, single-arm trial. Eligible patients were 18 years of age or older with Philadelphia chromosome negative ALL in second or greater relapse or whose disease progressed after two or greater treatment lines of anti-leukemia therapy. Patients received intravenous MARQIBO monotherapy at 2.25 mg/m2 over 60 minutes every seven days. The treated population included 65 patients who received at least one dose of MARQIBO. Of the 65 evaluable patients, three (4.6%) achieved complete remission, or CR, seven (10.8%) achieved complete remission with incomplete blood count recovery, or CRi, for a total of 10 (15.4%) total patients receiving a CR or CRi.

In addition to its approved indication, MARQIBO is being investigated in pediatric ALL in a Phase 1 investigator-initiated study in the United States. Based on data from this study, Spectrum will determine whether to conduct a registration study for MARQIBO in this setting. We are in discussions with the FDA regarding the possibility of using this development plan to satisfy one of the post-marketing requirements for the accelerated approval of our currently marketed indication for MARQIBO.

MARQIBO is also being investigated in diffuse large B-cell lymphoma in a Phase 3 investigator-initiated study in Europe in combination with the standard CHOP chemotherapy regimen in Europe, CHOP-14. Based on interim data from this study, Spectrum will consider whether to conduct a study of the combination of MARQIBO with the standard CHOP regimen in the United States, CHOP-21.

BELEODAQ

BELEODAQ (belinostat) is a histone deacytelase, or HDAC, inhibitor for the treatment of patients with relapsed or refractory PTCL. This indication was FDA approved in July 2014 under its accelerated approval program, based on tumor response rate and duration of response. BELEODAQ's anticancer effect is thought to be mediated through multiple mechanisms of action, including the inhibition of cell proliferation, induction of apoptosis (programmed cell death), inhibition of

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angiogenesis, induction of differentiation, and the activity in tumors that had become resistant to anticancer agents such as the platinums, taxanes, and topoisomerase II inhibitors.

The safety and effectiveness of BELEODAQ was evaluated in an open-label, single-arm, non-randomized international trial involving 129 participants with relapsed or refractory PTCL. Patients were treated with BELEODAQ 1,000 mg/m2 administered over 30 minutes via IV infusion once daily on days one to five of a 21-day cycle until disease progression or unacceptable toxicity. The primary efficacy endpoint was response rate (complete response and partial response) as assessed by an independent review committee, or IRC, using the International Workshop Criteria, or IWC. In all evaluable patients (N = 120) treated with BELEODAQ, the overall response rate per central review using IWC was 25.8%.

We market FOLOTYN and BELEODAQ for the treatment of relapsed or refractory PTCL. These drugs have different mechanisms of action, and as a result, the treating physician may prefer to start treatment with one drug over the other. In addition, physicians may prefer one drug over another based on specific patient factors such as the subtype of PTCL being treated, existing comorbidities, or the performance status of the patient. However, both drugs have similar response rates of approximately 25-30%. It is common for patients to cycle through multiple drugs, including both FOLOTYN and BELEODAQ, though these drugs are not FDA-approved for use in combination with one another.

In addition to its approved indication, BELEODAQ has been investigated in a Phase 1 study in combination with the CHOP chemotherapy regimen. Once the proper dose of FOLOTYN in combination with CHOP has been determined, we expect to plan a Phase 3 study of the combination of BELEODAQ and CHOP and FOLOTYN and CHOP, compared to CHOP alone for the treatment of first line PTCL. The Phase 1 study and the Phase 3 study concept are also the current post-marketing requirements for the FDA's accelerated approval of our currently marketed indication for BELEODAQ.

EVOMELA (previously referred to as Captisol-Enabled® MELPHALAN)

EVOMELA is intended for use as a high-dose conditioning treatment prior to autologous stem cell transplant, or ASCT, for patients with MM. MM is a cancer of plasma cells, a type of white blood cell present mainly in the bone marrow that produces antibodies. In MM, a group of plasma cells (myeloma cells) become cancerous and multiply, raising the number of plasma cells to a higher-than-normal level, which can crowd out normal blood cells and lead to abnormally high proteins in the blood or urine. The NCI estimated 30,000 new cases of MM in the U.S. in 2016, with the incidence of new cases increasing by approximately 2% per year.

The EVOMELA formulation avoids the use of propylene glycol, or PG, which is required as a co-solvent in the currently-available formulation of this product. The use of Betadex Sulfobutyl Ether Sodium technology to reformulate EVOMELA may allow for longer administration durations and slower infusion rates, potentially enabling clinicians to avoid reductions.

On March 10, 2016, the FDA approved EVOMELA as a high-dose conditioning treatment prior to hematopoietic progenitor (stem) cell transplantation in patients with MM, and for the palliative treatment of patients with MM for whom oral therapy is not appropriate. In April 2016, we launched EVOMELA, our sixth anti-cancer drug, with our existing sales force. On April 12, 2016, the FDA granted orphan drug exclusivity to EVOMELA, giving us seven years of marketing exclusivity until March 10, 2023. We also have two composition of matter patents that do not expire until March 2029.

EVOMELA was approved by the FDA based on its bioequivalence to the standard melphalan formulation (Alkeran) via the new drug regulatory pathway provided by Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act. The safety and effectiveness of EVOMELA in high-dose conditioning treatment was evaluated in an open-label, single-arm, non-randomized trial. The objective of the trial was to determine the overall safety and toxicity profile of 200 mg/m2 of EVOMELA in patients with MM undergoing ASCT. The overall response rate (partial response or better) improved from 79% prior to the ASCT procedure to 95% at 90 to 100 days post-transplant. There was also an

increase in the number of patients with a stringent complete response from zero patients prior to the ASCT procedure to 16% at 90 to 100 days post-transplant. Myeloablation, neutrophil engraftment, and platelet engraftment were achieved by all 61 patients. Myeloablation occurred on day five of ASCT (range ASCT days -one to six) with the median time to myeloablation from dosing of eight days. The median time to neutrophil engraftment was 12 days (range ASCT days 10 to 16). The median time to platelet engraftment was 13 days (range ASCT days 10 to 28).

New Product Pipeline

ROLONTIS

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ROLONTIS is being investigated for the treatment of chemotherapy-induced neutropenia. In January 2012, we entered into a co-development and commercialization agreement for worldwide rights, except for Korea, China, and Japan, with Hanmi Pharmaceutical Co., Ltd., or Hanmi, for ROLONTIS based on Hanmi's proprietary LAPSCOVERY Technology. Chemotherapy can cause myelosuppression and unacceptably low levels of white blood cells, making patients prone to infections, hospitalizations, and interruption of chemotherapy treatments. Neutropenia, a common side effect of chemotherapy, is a condition where the number of neutrophils or white blood cells are too low, and can lead to infection, hospitalization, and even death. Granulocyte colony-stimulating factor, or G-CSF, stimulates the production of white blood cells by the bone marrow. A recombinant form of G-CSF is used in appropriate cancer patients to accelerate recovery from neutropenia after chemotherapy, allowing higher-intensity treatment regimens to be given at full-dose and on schedule. We believe the worldwide annual market opportunity for G-CSF-related drugs is over $6 billion.

A Phase 2 clinical study of ROLONTIS was completed. This study assessed the effect of three different doses of this compound relative to pegfilgrastim (Neulasta, an approved long lasting G-CSF). The primary endpoint of the study was the duration of severe neutropenia (defined as absolute neutrophil count is $<0.5x10^9/L$) during Cycle 1 in patients with early stage breast cancer who are treated with docetaxel and cyclophosphamide (TC). The Phase 2 study demonstrated ROLONTIS to be non-inferior to 6 mg of pegfilgrastim at the 135 mcg/kg dose (0.44 days versus 0.31 days) and superior to pegfilgrastim at the 270 mcg/kg dose (0.03 days versus 0.31 days). The adverse event incidences were comparable to pegfilgrastim in all doses tested.

In September 2014, we announced our decision to advance ROLONTIS to Phase 3 trials due to the positive Phase 2 results in our collaboration program with Hanmi, and began discussions with the FDA and the European Medicines Agency, or EMA, to discuss our Phase 3 trial design. In December 2015, we reached agreement with the FDA regarding our Phase 3 Special Protocol Assessment, or SPA, for ROLONTIS. This pivotal Phase 3 study (ADVANCE Study, or SPI-GCF-301) was initiated in the first quarter of 2016 to evaluate ROLONTIS as a treatment for chemotherapy-induced neutropenia in patients with breast cancer. The study uses a fixed dose of ROLONTIS and is randomized to be compared to Neulasta with non-inferiority of duration of severe neutropenia as the primary endpoint. This study will be conducted in the United States, Canada, and South Korea. A second pivotal Phase 3 study (RECOVER Study, or SPI-GCF-302) with an identical study design is also planned. This study will enroll patients globally including in Europe and the United States.

QAPZOLA

QAPZOLA is a bio-reductive alkylating indoloquinone that is enzymatically activated by enzymes that are over expressed by bladder tumors that is being tested in NMIBC.

The NCI estimates that the 2016 incidence and prevalence of bladder cancer in the U.S. was approximately 77,000 cases. The global presence of bladder cancer is estimated at 2.7 million cases. According to Botteman et al., (PharmacoEconomics 2003), bladder cancer is the most expensive cancer to treat on a lifetime basis. The overall cost of bladder cancer treatment in the U.S. is approximately $3.4 billion annually, most of which is related to the direct treatment of this disease.

The initial treatment of bladder cancer is to attempt a complete surgical removal of the tumor. However, bladder cancer is a highly recurrent disease with approximately 80% of patients recurring within five years, and a majority of patients recurring within two years. This high recurrence rate is attributed to:

- the highly implantable nature of cancer cells that are dispersed during surgery;
- incomplete tumor resection; and
- tumors present in multiple locations in the bladder which may be missed or too small to visualize at the time of resection.

Despite evidence in the published literature and guidance from the American and European Urology Associations, instillation of a chemotherapeutic agent immediately following surgery is not a standard clinical practice. Currently, there are no FDA approved drugs for this indication which may, in part, explain the difference between the literature and urology guidelines and actual clinical management of this disease. For more than 30 years, no new drugs have

been introduced in the market for treatment of NMIBC. QAPZOLA represents much needed therapy for patients and may provide a meaningful opportunity to reduce overall medical costs.

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Pharmacokinetic studies have verified that QAPZOLA is rarely detectable in the bloodstream of patients when it is administered either after surgical resection or as a part of a delayed multi-instillation protocol. QAPZOLA is inactivated in the systemic circulation by the red blood cell fraction. The proposed dose therefore carries a minimal risk of systemic toxicity that could arise from absorption of a drug through the bladder wall into the bloodstream. An immediate instillation of QAPZOLA may help by:

- reducing tumor recurrence by destroying dispersed cancer cells that would otherwise re-implant onto the inner lining of the bladder;
- destroying remaining cancer cells at the site of tumor resection (also known as chemo-resection); and
- destroying tumors not observed during resection (also known as chemo-ablation).

We submitted a New Drug Application, or NDA, on December 11, 2015 which was accepted on February 9, 2016. On November 17, 2016, we received a Complete Response Letter, or CRL. We have since developed a new Phase 3 study for QAPZOLA, and in February 2017, we received a SPA from the FDA. The new Phase 3 study has been specifically designed to build on learnings from the previous studies as well as recommendations from the FDA. Compared to the previous study, this study will use twice the dosage of QAPZOLA (8mg), will evaluate approximately 70% fewer patients (n=425), and will also evaluate time-to-recurrence as the primary endpoint compared to recurrence at two years.

POZIOTINIB

POZIOTINIB is a novel, oral pan-HER inhibitor that irreversibly blocks signaling through the Epidermal Growth Factor Receptor (EGFR, HER) Family of tyrosine-kinase receptors, including HER1 (erbB1; EGFR), HER2 (erbB2), HER4 (erbB4), and HER receptor mutations. This, in turn, leads to the inhibition of the proliferation of tumor cells that over-express these receptors. Mutations or over-expression/amplification of EGFR family receptors have been associated with a number of different cancers, including non-small cell lung cancer, breast cancer, and gastric cancer. POZIOTINIB has shown single agent activity in the treatment of various cancer types, including breast, gastric, colorectal and lung cancers. In two Phase 1 studies for this drug that enrolled a variety of solid tumor patients and tested a variety of doses and schedules for POZIOTINIB, 6 of 10 breast cancer patients who failed at least two prior lines of anti-HER2 therapy demonstrated a partial response. The safety profile was consistent with similar drugs in this class with four patients having a grade 3 diarrhea response.

In November 2015, we submitted an Investigational New Drug, or IND, application with the FDA. In March 2016, we initiated a Phase 2 Breast Cancer Trial. The Phase 2 study (SPI-POZ-201) is an open-label study that will enroll approximately 75 patients with HER-2 positive metastatic breast cancer, who have failed at least two and no more than four HER-2 directed therapies. The dose and schedule of oral POZIOTINIB is based on clinical experience from the studies in South Korea, and in addition, include the use of prophylactic therapies to help minimize known side-effects of pan-HER directed therapies.

In collaboration with The University of Texas MD Anderson Cancer Center, an investigator sponsored trial is being initiated in non-small cell lung cancer patients with EGFR Exon 20 insertion mutations. The study is expected to yield results before December 31, 2017.

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For information on operating revenue related to the Company's principal products, as well as net loss, see Item 8 of Part II to this Annual Report on Form 10-K. Additionally, for information regarding possible adverse events or safety concerns regarding our commercialized and development stage products, see Item 1A. Risk Factors - Reports of adverse events or safety concerns involving each of our products or similar agents, sold by us or our development partners and/or licensees, could delay or prevent us from obtaining or maintaining regulatory approval or negatively impact sales.

Manufacturing

We currently do not have internal manufacturing capabilities; therefore, all of our products are manufactured on a contract basis. We expect to continue to contract with third-party providers for manufacturing and packaging services, including active pharmaceutical ingredients, or API, and finished-dosage products. We believe that our current agreements with third-party manufacturers provide for sufficient operating capacity to support the anticipated commercial demand and clinical requirements for our products. However, we are actively seeking multiple supplier sources for all our drug products in order to mitigate the risk of over-reliance on any one supplier. We attempt to prevent supply disruption through supply agreements, appropriate forecasting, and maintaining base stock levels. We believe that we could quickly enter into another supply or manufacturing agreement on substantially similar terms if we were required to do so.

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Sales and Marketing

We presently market and sell our pharmaceutical products through a direct sales force in the U.S., and through distributors in Europe (and previously in Japan). Our U.S. sales team is divided between “corporate accounts” and “oncology accounts” that generally serve different end-user types. The primary decision makers for our products are oncologists and hematologists. As of December 31, 2016, our U.S. sales force (sales management, sales representatives, and sales administrative support) numbered 92 employees.

Customers

Our product sales are concentrated to large pharmaceutical distributors (that ship and bill to hospitals and clinics). The customers that represent 10% or more of our total gross product sales in 2016, 2015, and 2014 are as follows:

	Product Sales		
	2016	2015	2014
AmerisourceBergen Corporation, and its affiliates	38.4%	36.7%	40.4%
McKesson Corporation and its affiliates	31.0%	34.2%	32.9%
Cardinal Health, Inc. and its affiliates	24.0%	17.4%	*

* Less than 10%

We are exposed to credit risk associated with trade receivables that result from these product sales. We do not require collateral or deposits from our customers due to our assessment of their creditworthiness and our long-standing relationship with them. We maintain reserves for potential bad debt, though credit losses have historically been nominal and within management’s expectations. A summary of our customers that represent 10% or more of our accounts receivables, net, as of December 31, 2016 and 2015 are as follows:

	Accounts Receivable, net	
	December 31, 2016	December 31, 2015
AmerisourceBergen Corporation, and its affiliates	33.9%	*
Cardinal Health, Inc. and its affiliates	33.0%	23.8 %
McKesson Corporation and its affiliates	26.1%	66.7 %

* Less than 10%

Competition

The pharmaceutical industry is characterized by rapidly-evolving biotechnology and intense competition, which we expect will continue. Many companies are engaged in research and development of compounds that are similar to ours – both commercialized and in development, which fosters continuous innovation. In the event that one or more of our competitor’s programs are successful, the market for some of our drug products could be reduced or eliminated. Any product for which we obtain FDA approval must also compete for market acceptance and market share.

Successful marketing of branded products depends primarily on the ability to communicate the effectiveness, safety, and value of the products to healthcare professionals in private practice, group practices, hospitals, academic institutions, and managed care organizations. Competition for branded drugs is less driven by price and is more focused on innovation in treatment of disease, advanced drug delivery, and specific clinical benefits over competitive drug therapies. Unless our products are shown to be differentiated, i.e., have a better safety profile, efficacy, and cost-effectiveness, as compared to other alternatives, they may not gain acceptance by medical professionals and may therefore never be commercially successful.

Companies that have products on the market or in research and development that target the same indications as our products include, among others, AstraZeneca plc, Bayer AG, Endo International plc, Eli Lilly and Company, Novartis International AG, Genentech, Inc. (Roche Holding AG), Bristol-Myers Squibb Company, Seattle Genetics, Inc.,

GlaxoSmithKline plc, Biogen Inc., OSI Pharmaceuticals, Inc. (Astellas Pharma Inc.), Cephalon, Inc. (Teva Pharmaceutical Industries Ltd.), Sanofi S.A., Pfizer, Inc., Merck & Company, Inc., Celgene Corporation, BiPar Sciences, Inc. (Sanofi S.A.), Sanofi Genzyme, Shire plc, AbbVie Inc., Poniard Pharmaceuticals, Inc., and Johnson & Johnson.

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Each of the aforementioned companies may be more advanced in development of competing drug products. Many of these competitors are large and well-capitalized companies focusing on a wide range of cancers and drug indications, and have substantially greater resources and expertise than we do.

We believe that the current competitive landscape for each of our commercialized products is as follows:

(a) FUSILEV is the levo-isomeric form of the racemic compound calcium, leucovorin, a product already approved for the same indication as FUSILEV. As there are currently four generic companies approved by the FDA to sell the leucovorin product, we are competing with a lower-cost alternative. For additional information, see the discussion under the heading Patents and Proprietary Rights below and Item 1A. Risk Factors -- Risks Related to Our Business -- Generic levo-leucovorin product competition could further adversely affect our FUSILEV revenues.

(b) ZEVALIN has two competitive products for its currently approved indications:

- Rituxan® (rituximab), marketed by Genentech Inc. and Biogen Inc., is indicated for the treatment of patients with relapsed or refractory, low-grade or follicular, CD20-positive, B-cell NHL as a single agent; previously untreated follicular, CD20-positive, B-cell NHL in combination with CVP (cyclophosphamide, vincristine and prednisone combination) chemotherapy; and non-progressing (including stable disease), low-grade, CD20-positive B-cell NHL, as a single agent, after first-line CVP chemotherapy. Rituxan is administered as a part of various chemotherapy regimens and schedules, the vast majority of which, could be used in concert with other therapeutic agents, such as ZEVALIN, as part of a treatment plan.

- Bendeka® (bendamustine hydrochloride) for Injection, for Intravenous Infusion, marketed by Teva Pharmaceutical Industries Ltd., is indicated for the treatment of patients with indolent B-cell NHL that has progressed during or within six months of treatment with rituximab or a rituximab-containing regimen.

(c) FOLOTYN, was the first agent approved by the FDA for treatment of patients with relapsed or refractory PTCL. BELEODAQ is a HDAC inhibitor, also indicated for the treatment of patients with relapsed or refractory PTCL. Both drugs were approved under accelerated approval based on tumor response rate. Clinical benefit such as improvement in progression-free survival or overall survival has not been demonstrated. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

There are many existing approaches used in the treatment of relapsed or refractory PTCL, including combination chemotherapy and single agent regimens, which represent competition for FOLOTYN and BELEODAQ. Both drugs have two primary competitive products for their currently approved indications:

- Istodax® (Romidepsin), marketed by Celgene Corporation, was granted accelerated approval by the FDA in June 2011 for the treatment of patients with PTCL who have received at least one prior therapy.

- Adcetris® (Brentuximab vedotin), marketed by Seattle Genetics, Inc., was granted accelerated approval by the FDA in August 2011 for the treatment of patients with systemic anaplastic large cell lymphoma, or ALCL, after failure of at least one prior multi-agent chemotherapy regimen. ALCL is one of the subtypes of PTCL included in the labels of FOLOTYN, BELEODAQ and Istodax.

We are aware of multiple investigational agents that are currently being studied in clinical trials for PTCL which, if approved, may compete with FOLOTYN and BELEODAQ. Many patients with PTCL do not adequately respond to a single treatment agent, so many patients receive treatment with more than one agent (e.g., BELEODAQ and FOLOTYN).

(d)

MARQIBO is a liposomal form of standard vincristine. In its current indication, MARQIBO is approved for adult patients with relapsed or refractory Ph-ALL who have not responded or relapsed after two prior treatments. This indication received the FDA's accelerated approval based on tumor response rate. Clinical benefit such as improvement in overall survival has not been verified. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

Currently, standard vincristine is not approved for the same indication as MARQIBO. However, there are many existing approaches used in the treatment of relapsed or refractory Ph-ALL, including combination chemotherapy and single agent regimens, which represent competition for MARQIBO. There are a variety of investigational agents in clinical trials for ALL that if approved could represent future competition for MARQIBO.

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Research and Development

New drug development is the process whereby drug product candidates are tested for the purpose of filing an NDA or a Biologics License Application, or BLA, in the U.S. (or similar filing in other countries). Obtaining marketing approval from the FDA or similar regulatory authorities outside of the U.S. is an inherently uncertain, lengthy, and expensive process that requires several phases of clinical trials to demonstrate to the satisfaction of the appropriate regulatory authorities that the products are both safe and effective for their respective indications. Our development focus is primarily based on acquiring and developing late-stage development drugs as compared to new drug discovery, which is particularly uncertain and lengthy.

Our in-development products are summarized below:

Our research and development expenses for drug development are comprised of our personnel expenses, contracted services with third parties, license fees and milestone payments to third parties, clinical trial costs, laboratory supplies, drug products, and certain allocations of corporate costs. The below table summarizes our research and development expenses by project in 2016, 2015, and 2014:

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	Research and Development Expenses for the Year Ended December 31, (in thousands)			
	2016		2015	2014	
ROLONTIS	$ 14,829	*	$ 1,133	$ 4,141	
QAPZOLA	5,437		4,147	1,377	
EVOMELA	4,964		8,568	5,966	
MARQIBO	4,249		4,412	6,623	
ZEVALIN	3,814		3,025	6,950	
LEVOLEUCOVORIN (new formulation)	2,667		—	—	
FOLOTYN	1,717		2,650	4,927	
POZIOTINIB	976		4,240	—	
BELEODAQ	772		1,320	20,911	**
FUSILEV	—		885	442	
Other in-development compounds and drugs	283		633	1,967	
Total — Direct costs	39,708		31,013	53,304	
Add: General research and development expenses (including personnel costs that correspond to more than one in-development project)	21,148		21,571	21,073	
(Less): Reimbursements from development partners of ROLONTIS and BELEODAQ	(1,710)		(521)	(2,758)	
(Less): Incurred FOLOTYN study costs that credit expense and reduce our drug development liability (see Note 16 to Consolidated Financial Statements)	(210)		(1,297)	(1,957)	
Total research and development expenses	$ 58,936		$ 50,766	$ 69,662	

* Inclusive of 2016 milestone payment of $2.7 million (see Note 17(xii) to the accompanying Consolidated Financial Statements).

** Inclusive of 2014 milestone payment of $17.8 million (see Note 17(xi) to the accompanying Consolidated Financial Statements).

Patents and Proprietary Rights

Our Patents and Proprietary Rights

We in-license from third parties certain patent and related intellectual property rights related to our proprietary drug products. Under most of these license arrangements, we are generally responsible for all development, patent filing and maintenance costs, sales, marketing and liability insurance costs related to the drug products.

In addition, these licenses and agreements may require us to make royalty and other payments and to reasonably utilize the underlying technology of applicable patents. If we fail to comply with these and other terms in these licenses and agreements, we could lose the underlying rights to one or more of our potential products, which would adversely affect our product development and harm our business.

The protection, preservation and infringement-free commercial utilization of these patents and related intellectual property rights are very important to the successful execution of our strategy. However, the issuance of a patent is neither conclusive as to its validity nor as to the enforceable scope of the claims of the patent. Accordingly, our patents and the patents we have licensed may not prevent other companies from developing similar or functionally equivalent products or from successfully challenging the validity of our patents. If our patent applications are not allowed or, even if allowed and issued as patents, if such patents or the patents we have in-licensed are circumvented or not upheld by the courts, our ability to competitively utilize our patented products and technologies may be significantly reduced. Also, such patents may or may not provide competitive advantages for their respective products or they may be challenged or circumvented by competitors, in which case our ability to commercially sell these products may be diminished.

From time-to-time, we may need to obtain licenses to patents and other proprietary rights held by third parties to develop, manufacture and market our products. If we are unable to timely obtain these licenses on commercially reasonable terms, our ability to commercially exploit such products may be inhibited or prevented.

We believe that our patents and licenses are critical to operating our business, as summarized below by commercialized and in-development drug products.

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FUSILEV: Fusilev had/has orphan drug exclusivity for two indications. These indications are for the treatment of (i) osteosarcoma (which expired on March 7, 2015) and (ii) mCRC (which expires on April 29, 2018). FUSILEV also had/has a U.S. composition of matter patent that expires in March 2022.
In February 2015, the U.S. District Court for the District of Nevada found the asserted claims of the patent covering FUSILEV to be invalid, and on October 2, 2015, the Court of Appeals for the Federal Circuit affirmed that decision. On April 27, 2015, we filed suit in the U.S. District Court for the District of Columbia against the FDA seeking a temporary restraining order or preliminary injunction to suspend FDA approval of Sandoz Inc.'s, or Sandoz, Abbreviated New Drug Application, or ANDA. We have contended that Sandoz's ANDA should not have been approved until the expiry of our Orphan Drug Exclusivity on April 29, 2018. On April 29, 2015, the court denied the temporary restraining order and on May 27, 2015, the court entered summary judgment in favor of the FDA et al. On June 5, 2015, we filed our Notice of Appeal. On June 3, 2016, the U.S. Court of Appeals for the District of Columbia affirmed the judgment in favor of the FDA et al.
ZEVALIN: We have sublicensed U.S. patents that cover the processes and tools for making monoclonal anti-bodies or MABs, in general, licensed U.S. patents that cover the CD-20 MAB in ZEVALIN as well as the use of ZEVALIN to treat NHL, and acquired patents covering the ZEVALIN compounding process (i.e., process of linking the CD-20 MAB to a radioactive isotope to make the patient-ready dosage form of ZEVALIN). These patents expire over a wide range of dates, and the licensed patents covering the CD-20 MAB began to expire in 2015. Additionally, we have U.S. patents covering the compounding process expiring in 2019, and we are considering filing new patent applications.
FOLOTYN: We have a composition of matter patent due to expire in 2022 following a five-year patent term extension in U.S. The composition of matter patent is due to expire in Europe in 2017 but is eligible for a similar patent term extension following regulatory approval in Europe. We also have patents covering the use of FOLOTYN for PTCL that will not expire until 2025. Additionally, we are considering filing new patent applications.
MARQIBO: We have U.S. and European patents covering the use of MARQIBO for leukemia, lymphoma and melanoma, and a U.S. patent covering the MARQIBO kit, all expiring in 2020. We have filed a patent cooperation treaty, or PCT, application claiming a method of encapsulating vincristine sulphate into liposomes. We are presently in the process of developing a “single vial” formulation of MARQIBO, and if we are successful, we believe our U.S. patent coverage could be extended to 2036.
BELEODAQ: The composition of matter patents that cover BELEODAQ and related compounds do not begin to expire until 2027. Currently, there are multiple U.S. and foreign patent applications pending that cover BELEODAQ formulations, uses and manufacturing and synthesis processes. We plan to file additional U.S. and foreign patent applications covering new formulations, uses, and manufacturing and synthesis processes.
EVOMELA: This drug is covered by issued patents claiming improved Captisol® technology that are due to expire between 2025 and 2029 in the U.S. Outside the U.S., we have issued patents that cover improved Captisol technology that are due to expire in 2025 and pending applications with anticipated expiry in 2029 (if issued). We also have filed patent applications covering Captisol-based formulation of EVOMELA in the U.S. and a number of other countries.
QAPZOLA: The U.S. formulation patent does not expire until 2022, and method of treatment of bladder cancer using a stabilized formulation that does not expire until 2024. Formulation patents outside the U.S. are due to expire in 2022. We have filed and plan to file additional U.S. and foreign patent applications covering new formulations and/or uses for this product.
ROLONTIS: Composition of matter patents covering ROLONTIS are due to expire in 2025 in the U.S. and in 2024 outside the U.S. ROLONTIS is also covered by additional patents claiming various aspects of the technology that are due to expire between 2024 and 2030 and we have filed patent applications for its formulation.

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We are constantly evaluating our patent portfolio and are currently assessing and filing patent applications for our drug products and considering new patent applications in order to maximize the life cycle of each of our products. While the U.S. and the European Union, or EU, are currently the largest potential markets for most of our products, we also have patents issued and patent applications pending outside of the U.S. and Europe. Limitations on patent

protection in these countries, and the differences in what constitutes patentable subject matter in countries outside the U.S., may limit the

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protection we have on patents issued or licensed to us outside of the U.S. In addition, laws of foreign countries may not protect our intellectual property to the same extent as would laws in the U.S.

To minimize our costs and expenses and to maintain effective protection, we usually focus our patent and licensing activities within the U.S., the EU, Canada, and Japan. In determining whether or not to seek a patent or to license any patent in a certain foreign country, we weigh the relevant costs and benefits, and consider, among other things, the market potential and profitability, the scope of patent protection afforded by the law of the jurisdiction and its enforceability, and the nature of terms with any potential licensees. Failure to obtain adequate patent protection for our proprietary drugs and technology would impair our ability to be commercially competitive in these markets.

In conducting our business, we rely upon trade secrets, know-how, and licensing arrangements. We use customary practices for the protection of our confidential and proprietary information such as confidentiality agreements and trade secret protection measures. It is possible that these agreements will be breached or will not be enforceable in every instance, and that we will not have adequate remedies for any such breach. It is also possible that our trade secrets or know-how will otherwise become known or independently developed by competitors. The protection of know-how is particularly important because it is often necessary or useful information that allows us to practice the claims in the patents related to our proprietary drug products.

In addition to the specific intellectual property subjects discussed above, we have trademark protection in the U.S. for Spectrum Pharmaceuticals, Inc.®, FUSILEV®, FOLOTYN®, ZEVALIN®, MARQIBO®, BELEODAQ®, and EVOMELA®. We also have trademarks in ROLONTIS™, QAPZOLA™, REDEFINING CANCER CARE™, and the Spectrum Pharmaceuticals' logos and have pending U.S. and ex-U.S. trademark applications for other potential marks.

The Patent Process

The U.S. Constitution provides Congress with the authority to provide inventors the exclusive right to their discoveries. Congress codified this right in U.S. Code Title 35, which gave the United States Patent and Trademark Office, or USPTO, the right to grant patents to inventors and defined the process for securing a U.S. patent. This process involves the filing of a patent application that instructs a person having ordinary skill in the respective art how to make and use the invention in clear and concise terms. The invention must be novel (i.e., not previously known) and non-obvious (i.e., not an obvious extension of what is already known). The patent application concludes with a series of claims that specifically describe the subject matter that the patent applicant considers his invention.

The USPTO undertakes an examination process that can take from one to seven years, or more, depending on the complexity of the patent and the problems encountered during examination.

In exchange for disclosing the invention to the public, for all U.S. patent applications filed after 1995, the successful patent applicant is currently provided a right to exclude others from making, using or selling the claimed invention for a period of 20 years from the effective filing date of the patent application.

Under certain circumstances, a patent term may be extended. Patent extensions are most frequently granted in the pharmaceutical and medical device industries under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, to recover some of the time lost during the FDA regulatory process, subject to a number of limitations and exceptions. The patent term may be extended up to a maximum of five years; however, as a general rule, the average extension period granted for a new drug is approximately three years. Only one patent can be extended per FDA approved product, and a patent can only be extended once.

Product Exclusivity

Under the Hatch-Waxman Act, drug products are provided exclusivity whereby the FDA will not accept applications to market a generic form of an innovator reference listed drug product until the end of the prescribed period. A product is granted a five-year period of exclusivity if it contains a chemical entity never previously approved by the FDA either alone or in combination, although generic applications may be submitted after four years if they contain a certification of patent invalidity or non-infringement as further discussed below. A three-year period of exclusivity is granted to a previously approved product based on certain changes (e.g., in strength, dosage form, route of administration or conditions of use), where the application is supported by new clinical investigations that are essential to approval. In addition, in 1997, Congress amended the law to provide an additional six months of

exclusivity as a reward for studying drugs in children. This pediatric exclusivity, which can be obtained during the approval process or after approval, effectively delays the approval of a generic application until six months after the expiration of any patent or other exclusivity that would otherwise delay approval, thus providing an additional

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six months free of generic competition. In order to qualify for pediatric exclusivity, the FDA must make a written request for pediatric studies, the application holder must agree to the request and complete the studies within the required timeframe, and the studies must be accepted by the FDA based on a determination that the studies fairly respond to the request. The provisions were enacted with a five-year sunset date, and have been reauthorized in 2002, 2007 and 2012.

Generic Approval and Patent Certification

The Hatch-Waxman Act also created the ANDA approval process, which permits the approval of a generic version of a previously approved branded drug without the submission of a full NDA, and based in part on the FDA's finding of safety and effectiveness for the reference listed drug. Applicants submitting an NDA are required to list patents associated with the drug product, which are published in the FDA Orange Book, and the timing of an ANDA approval depends in part on patent protection for the branded drug. When an ANDA is filed, the applicant must file a certification for each of the listed patents for the branded drug, stating one of the following: (1) that there is no patent information listed; (2) that such patent has expired; (3) that the patent will expire on a particular date (indicating that the ANDA may be approved on that date); or (4) that the drug for which approval is sought either does not infringe the patent or the patent is invalid, otherwise known as paragraph IV certification. If an ANDA applicant files a paragraph IV certification, it is required to provide the patent holder with notice of that certification. If the patent holder brings suit against the ANDA applicant for patent infringement within 45 days of receiving notice, the FDA may not approve the ANDA until the earlier of (i) 30 months from the patent holder's receipt of the notice (the 30-month stay) or (ii) the issuance of a final, non-appealed, or non-appealable court decision finding the patent invalid, unenforceable or not infringed.

The Hatch-Waxman Act also provided an incentive for generic manufacturers to file paragraph IV certifications challenging patents that may be invalid, unenforceable, or not infringed, whereby the first company to successfully challenge a listed patent and receive ANDA approval is protected from competition from subsequent generic versions of the same drug product for up to 180 days after the earlier of (1) the date of the first commercial marketing of the first-filed ANDA applicant's generic drug or (2) the date of a decision of a court in an action holding the relevant patent invalid, unenforceable, or not infringed. These 180-day exclusivity provisions have been the subject of litigation and administrative review, and the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or MMA, amended the provisions in several ways, including by providing that an ANDA applicant entitled to 180-day exclusivity may lose such exclusivity if any of the following events occur: (1) failure to market; (2) withdrawal of the ANDA; (3) change in patent certification; (4) failure to obtain tentative approval; (5) illegal settlement agreement; or (6) patent expiration.

With respect to the illegal settlement prong, the MMA amendments require that certain types of settlement agreements entered into between branded and generic pharmaceutical companies related to the manufacture, marketing and sale of generic versions of branded drugs are required to be filed with the Federal Trade Commission and the Department of Justice for review of potential anti-competitive practices. This requirement could affect the manner in which generic drug manufacturers resolve intellectual property litigation and other disputes with branded pharmaceutical companies, and could result generally in an increase in private-party litigation against pharmaceutical companies. The impact of this requirement, and the potential governmental investigations and private-party lawsuits associated with arrangements between brand name and generic drug manufacturers, remains uncertain. In addition, Congress has considered enacting legislation that would prohibit such settlements between brand name and generic drug manufacturers. Such a provision was considered as part of the Patient Protection and Affordable Care Act, or PPACA, signed into law on March 23, 2010. However, Congress removed the provision prior to passage. It is possible that Congress will again consider a ban on such settlements between brand name and generic drug manufacturers in the future.

The PPACA provides exclusivity protections for certain innovator biological products and a framework for FDA review and approval of biosimilar and interchangeable versions of innovator biologic products. The PPACA provides that no application for a biosimilar product may be approved until 12 years after the date on which the innovator

product was first licensed, and no application may be submitted until four years after the date of first licensure. Products deemed interchangeable (as opposed to biosimilar) are also eligible for certain exclusivity.

Orphan Drug Designation

Some jurisdictions, including Europe and the U.S., may designate drugs for relatively small patient populations as "orphan" drugs. The FDA may grant orphan drug designation to a drug intended to treat a rare disease or condition that affects fewer than 200,000 individuals in the U.S., and a drug may also be considered an orphan even if the drug treats a disease or condition affecting more than 200,000 individuals in the U.S. Orphan drug designation does not necessarily convey any advantage in, or shorten the duration of, the regulatory review and process for marketing approval. If a product with an orphan drug designation subsequently receives the first FDA approval for the indication for which it has such designation, the product

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is entitled to seven years of orphan drug exclusivity, during which time the FDA will not approve any other application to market the same drug for the same indication except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity. Also, competitors are not prohibited from receiving approval to market the same drug or biologic for a different indication than that which received orphan approval.
Under EU medicines laws, the criteria for designating an "orphan medicinal product" are similar in principle to those in the U.S. Criteria for orphan designation are set out in Article 3 of Regulation (EC) 141/2000 on the basis of two alternative conditions. A medicinal product may be designated as orphan if it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the EU, when the application is made. This is commonly known as the "disease prevalence criterion" Alternatively, a product may be so designated if it is intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition in the EU and if without incentives it is unlikely that the marketing of the product in the EU would generate sufficient return to justify the necessary investment. This is commonly known as the "insufficient return criterion."

These two alternative criteria must cumulatively meet the second condition that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the EU, or if such a method exists, the product will be of significant benefit to those affected by the condition. "Significant benefit" is defined in Regulation (EC) 847/2000 as a clinically relevant advantage or a major contribution to patient care.
Upon grant of a marketing authorization, orphan medicinal products are entitled to ten years of market exclusivity in respect of the approved therapeutic indication. Within the period of market exclusivity, no competent authority in the EU is permitted to accept an application for marketing authorization, a variation or a line-extension for the same approved therapeutic indication in respect of a similar medicinal product pursuant to Article 8.1 of Regulation 141/2000 unless one of the derogations set out in Article 8.3 of the same Regulation applies. In order to determine whether two products are considered similar, Regulation 847/2000 requires an assessment of the principal molecular structure and the underlying mode of action. Any minor variation or modification of the principal molecular structure would not ordinarily render the second product dissimilar to the first authorized product.
In order for the second applicant to break the market exclusivity granted to the first authorized similar medicinal product in respect of the same therapeutic indication, the second applicant would principally rely upon data to demonstrate that its product is safer, more efficacious or clinically superior to the first product pursuant to Article 8.3I of Regulation 141/2000. Ordinarily, such an assessment will require a head-to-head comparative clinical trial for the purpose of demonstrating clinical superiority.
The 10-year market exclusivity may be reduced to six years if at the end of the fifth year it is established that the product no longer meets the criteria for orphan designation on the basis of available evidence. To date, each of our six commercialized drugs continues to meet the orphan drug designation requirements.

FUSILEV had/has been granted orphan drug designations for its use in conjunction with high dose MTX in the treatment of osteosarcoma and for its use in combination chemotherapy with the approved agent 5-fluorouracil in the palliative treatment of metastatic adenocarcinoma of the colon and rectum (colorectal cancer). In addition, FOLOTYN has been granted an orphan drug designation for the treatment of T-cell lymphoma and BELEODAQ has been granted an orphan drug designation for PTCL. Lastly, MARQIBO has been granted orphan drug designations for its use in the treatment of adult patients with ALL in second or greater relapse or whose disease has progressed following two or more anti-leukemia therapies, and ZEVALIN has orphan drug designations for the treatment of patients with relapsed or refractory low-grade, follicular, or transformed B-cell NHL, including patients with Rituximab refractory follicular NHL.

Governmental Regulation

The development, production and marketing of our proprietary and generic drug and biologic products are subject to regulation for safety, efficacy and quality by numerous governmental authorities in the U.S. and other countries. In the U.S., drugs and biologics are subject to rigorous regulation. The Federal Food, Drug, and Cosmetic Act, as amended from time to time, and the regulations promulgated thereunder, as well as other federal and state statutes and

regulations, govern, among other things, the development, approval, manufacture, safety, labeling, storage, record keeping, distribution, promotion, and advertising of our products. Product development and approval within this regulatory framework, including for drugs already at a clinical stage of development, can take many years and require the expenditure of substantial resources, and to obtain FDA approval, a product must satisfy mandatory quality, safety, and efficacy requirements. In addition, each drug-manufacturing establishment must be registered with the FDA. Domestic manufacturing establishments must comply with the FDA's current Good Manufacturing Practices, or cGMP, regulations and are subject to inspections by the FDA. To supply drug ingredients or

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products for use in the U.S., foreign manufacturing establishments must also comply with cGMP and are subject to inspections by the FDA or by other regulatory authorities in certain countries under reciprocal agreements with the FDA.

General Information about the Drug Approval Process and Post-Marketing Requirements

The U.S. system of new drug and biologics approval is a rigorous process. Only a small percentage of compounds that enter the pre-clinical testing stage are ever approved for commercialization. Our strategy focuses on in-licensing clinical stage drug products that are already in or about to enter human clinical trials. A late-stage focus helps us to effectively manage the high cost of drug development by focusing on compounds that have already passed the many hurdles in the pre-clinical and early clinical process.

The following general comments about the drug approval process are relevant to the development activities we are undertaking with our proprietary products.

Pre-clinical Testing: During the pre-clinical testing stage, laboratory and animal studies are conducted to show biological activity of a drug or biologic compound against the targeted disease. The compound is evaluated for safety. While all of our compounds are currently in clinical trials, it is possible that additional pre-clinical testing could be requested by a regulatory authority for any of our compounds.

Investigational New Drug Application: After certain pre-clinical studies are completed, an IND application is submitted to the FDA to request the ability to begin human testing of the drug or biologic. An IND becomes effective thirty days after the FDA receives the application (unless the FDA notifies the sponsor of a clinical hold), or upon prior notification by the FDA.

Phase 1 Clinical Trials: These trials typically involve small numbers of healthy volunteers or patients and usually define a drug candidate’s safety profile, including the safe dosage range.

Phase 2 Clinical Trials: In Phase 2 clinical trials, controlled studies of human patients with the targeted disease are conducted to assess the drug’s effectiveness. These studies are designed primarily to determine the appropriate dose levels, dose schedules and route(s) of administration, and to evaluate the effectiveness of the drug or biologic on humans, as well as to determine if there are any side effects on humans to expand the safety profile following Phase 1. These clinical trials, and Phase 3 trials discussed below, are designed to evaluate the product’s overall benefit-risk profile, and to provide information for physician labeling.

Phase 3 Clinical Trials: This phase usually involves a larger number of patients with the targeted disease. Investigators (typically physicians) monitor the patients to determine the drug candidate’s efficacy and to observe and report any adverse reactions that may result from long-term use of the drug on a large, more widespread, patient population. During the Phase 3 clinical trials, typically the drug candidate is compared to either a placebo or a standard treatment for the target disease.

New Drug Application or Biologics License Application: After completion of all three clinical trial Phases, if the data indicates that the drug is safe and effective, an NDA or BLA is filed with the FDA requesting FDA approval to market the new drug as a treatment for the target disease.

Fast Track and Priority Review: The FDA has established procedures for accelerating the approval of drugs to be marketed for serious or life threatening diseases for which the manufacturer can demonstrate the potential to address unmet medical needs.

Abbreviated New Drug Application: An ANDA is an abbreviated new drug application for generic drugs created by the Hatch-Waxman Act. When a company files an ANDA, it must make a patent certification regarding the patents covering the branded product listed in the FDA’s Orange Book. The ANDA drug development process generally takes less time than the NDA drug development process since the ANDA process usually does not require new clinical trials establishing the safety and efficacy of the drug product.

NDA/BLA and ANDA Approval: The FDA approves drugs and biologics that are subject to NDA and BLA review based on data in the application demonstrating the product is safe and effective in its proposed use(s) and that the product’s benefits outweigh its risks. The FDA will also review the NDA or BLA applicant’s manufacturing process and controls to ensure they are adequate to preserve the drug’s identity, strength, quality, and purity. Finally, the FDA

will review and approve the product's proposed labeling. As for the ANDA approval process, these "abbreviated" applications are generally not required to include preclinical or clinical data to establish safety and effectiveness. Rather, an ANDA must demonstrate both chemical equivalence

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and bio-equivalence (the rate and extent of absorption in the body) to the innovator drug — unless a bio-equivalence waiver is granted by the FDA.

Phase 4 Clinical Trials: After a drug has been approved by the FDA, Phase 4 studies may be conducted to explore additional patient populations, compare the drug to a competitor, or to further study the risks, benefits and optimal use of a drug. These studies may be a requirement as a condition of the initial approval of the NDA or BLA.

Post-Approval Studies Requirements under FDAAA: The Food and Drug Administration Amendments Act of 2007, or FDAAA, significantly added to the FDA's authority to require post-approval studies. Under the FDAAA, if the FDA becomes aware of new safety information after approval of a product, they may require us to conduct further clinical trials to assess a known serious risk, signals of serious risk or to identify an unexpected serious risk. If required to conduct a post-approval study, periodic status reports must be submitted to the FDA. Failure to conduct such post-approval studies in a timely manner may result in administrative action being taken by FDA, including substantial civil fines.

Risk Evaluation and Mitigation Strategy Authority under FDAAA: The FDAAA also gave the FDA new authority to require the implementation of a Risk Evaluation and Mitigation Strategy, or REMS, for a product when necessary to minimize known and preventable safety risks associated with the product. The FDA may require the submission of a REMS before a product is approved, or after approval based on "new safety information," including new analyses of existing safety information. A REMS may include a medication guide, patient package insert, a plan for communication with healthcare providers, or other elements as the FDA deems are necessary to assure safe use of the product, which could include imposing certain restrictions on distribution or use of a product. A REMS must include a timetable for submission of assessments of the strategy at specified time intervals. Failure to comply with a REMS, including the submission of a required assessment, may result in substantial civil or criminal penalties.

Other Issues Related to Product Safety: Adverse events that are reported after marketing approval also can result in additional limitations being placed on a product's use and, potentially, withdrawal of the product from the market. In addition, under the FDAAA, the FDA has authority to mandate labeling changes to products at any point in a product's lifecycle based on new safety information derived from clinical trials, post-approval studies, peer-reviewed medical literature, or post-market risk identification and analysis systems data.

FDA Enforcement

The development of drug and biologic products, as well as the marketing of approved drugs and biologics, is subject to substantial continuing regulation by the FDA, including regulation of adverse event reporting, manufacturing practices and the advertising and promotion of the product. Failure to comply with the FDA and other governmental regulations can result in fines, unanticipated compliance expenditures, recall or seizure of products, total or partial suspension of production and/or distribution, suspension of the FDA's review of NDAs, BLAs, ANDAs or other product applications, enforcement actions, injunctions and criminal prosecution. Under certain circumstances, the FDA also has the authority to revoke previously granted drug approvals.

With respect specifically to information submitted to the FDA in support of marketing applications, the FDA, under its Fraud, Untrue Statements of Material Facts, Bribery and Illegal Gratuities Policy, can significantly delay the approval of a marketing application, or seek to withdraw an approved application where it identifies fraud or discrepancies in regulatory submissions. Such actions by the FDA may significantly delay or suspend substantive scientific review of a pending application during validity assessment or remove approved products from the market until the assessment is complete and questions regarding reliability of the data are resolved. In addition, the Generic Drug Enforcement Act of 1992 established penalties for wrongdoing in connection with the development or submission of an ANDA. Under this Act, the FDA has the authority to permanently or temporarily bar companies or individuals from submitting or assisting in the submission of an ANDA, and to temporarily deny approval and suspend applications to market generic drugs. The FDA may also suspend the distribution of all drugs approved or developed in connection with certain wrongful conduct and/or withdraw approval of an ANDA and seek civil penalties.

Healthcare Reform

Continuing studies of the proper utilization, safety and efficacy of pharmaceuticals and other health care products are being conducted by industry, government agencies and others. Such studies, which increasingly employ sophisticated methods and techniques, can call into question the utilization, safety and efficacy of previously marketed products and in some cases have resulted, and may in the future result, in the discontinuance of their marketing.

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The Patient Centered Outcomes Research Institute, or the Institute, a private, non-profit corporation created as a result of the PPACA, is tasked with assisting patients, clinicians, purchasers, and policy-makers in making informed health decisions. One of the Institute's initiatives will be to conduct comparative clinical effectiveness research, which is defined as "research evaluating and comparing health outcomes and the clinical effectiveness, risks, and benefits of two or more medical treatments, services, and items." It is important to note that the Institute would not be permitted to mandate coverage, reimbursement, or other policies for any public or private payer, however, the outcome of the Institute's initiatives could influence prescriber behavior.

Foreign Regulation

Whether or not we obtain FDA approval for a product, we must obtain approval of a product by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of the product in those countries. The approval process varies from country/region to country/region, and the time may be longer or shorter than that required for FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement also may vary, sometimes significantly, from country/region to country/region.

Under the EU regulatory systems, we may submit marketing authorization applications either under a centralized procedure or decentralized procedure or the mutual recognition procedure. The centralized procedure is mandatory for medicines produced by a biotechnological process. The procedure is also mandatory for new active substances which are indicated for treatment of several diseases or conditions, including cancer and orphan conditions. Companies may apply for centralized assessment if the product contains a new active substance or the product constitutes significant therapeutic, scientific or technical innovation or the granting of authorization under the centralized procedure is in the interests of the EU patients. A centralized marketing authorization is valid in all EU member states. This marketing authorization is issued in the form of a European Commission decision which is legally binding in its entirety to which it is addressed.

Directive 2004/27/EC introduced two parallel procedures to the centralized procedure to allow a product to be progressively authorized in each of the member states of the EU. They are the decentralized procedure and the mutual recognition procedure. The mutual recognition procedure applies where the product has already been authorized in a member state of the EU that will act as reference member state. The national marketing authorization granted by the reference member state forms the basis for mutual recognition in the member states chosen by the applicant. In the decentralized procedure, the product in question is not authorized in any one the EU member states. In such a situation, the applicant company will request a member state to act as the reference member state to lead the scientific assessment for the benefit/risk balance for agreement by the concerned member states. In both cases, the concerned member states have up to 90 days to accept or raise reasoned objections to the assessment made by the reference member state.

In addition, pricing and reimbursement is subject to negotiation and regulation in most countries outside the U.S. Increasingly, adoption of a new product for use in national health services is subject to health technology assessment under the national rules and regulations to establish the clinical effectiveness and cost-effectiveness of a new treatment. In some countries, in order to contain health care expenditures, reference price is introduced in order for the national healthcare providers to achieve a price comparable to the reference price in the same therapeutic category. We may therefore face the risk that the resulting prices would be insufficient to generate an acceptable return to us.

Third Party Reimbursement and Pricing Controls

In the U.S. and elsewhere, sales of pharmaceutical products depend in significant part on the availability of reimbursement to the consumer from third-party payers, such as government and private insurance plans. Third-party payers are increasingly challenging the prices charged for medical products and services. It is time-consuming and expensive for us to go through the process of seeking reimbursement from Medicare and private payers. Our products may not be considered cost effective, and coverage and reimbursement may not be available or sufficient to allow us to sell our products on a competitive and profitable basis.

The PPACA enacted significant reforms, including revising the definition of "average manufacturer price" for reporting purposes, increasing Medicaid rebates, expanding the 340B drug discount program, and making changes to affect the

Medicare Part D coverage gap, or “donut hole.” In the coming years, additional significant changes could be made to governmental healthcare programs, and the U.S. healthcare system as a whole, that may result in significantly increased rebates, decreased pricing flexibility, diminished negotiating flexibility, coverage and reimbursement limitations based upon comparative and cost-effectiveness reviews, and other measures that could significantly impact the success of our products.

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In many foreign markets, including the countries in the EU, pricing of pharmaceutical products is subject to governmental control. In the U.S., there have been, and we expect that there will continue to be, a number of federal and state proposals to implement similar governmental pricing control.

Employees

As of December 31, 2016, we had 227 employees (as compared to 212 employees as of December 31, 2015), 8 of whom hold an M.D. degree, and 20 of whom hold a Ph.D. degree. We believe that the success of our business will depend, in part, on our ability to attract and retain uniquely qualified personnel. Our employees are not part of any collective bargaining agreements, and we believe that we have good relations with our employees.

General Information

We are a Delaware corporation. We originally incorporated in Colorado in December 1987 as Americus Funding Corporation. We changed our corporate name in August 1996 to NeoTherapeutics, Inc., and reincorporated in Delaware in June 1997. We changed our corporate name in December 2002 to Spectrum Pharmaceuticals, Inc.

Our principal executive office is located at 11500 South Eastern Avenue, Suite 240, Henderson, Nevada 89052. Our telephone number is (702) 835-6300. Our website is located at www.sppirx.com. The information that can be accessed through our website is not incorporated by reference into this Annual Report on Form 10-K and should not be considered to be a part hereof.

We make our proxy statements, annual reports on Form 10-K, quarterly reports on Form 10-Q, and current reports on Form 8-K (and related amendments to these reports, as applicable) available on our website free of charge as soon as practicable after filing or furnishing with the Securities and Exchange Commission, or the SEC.

All such reports are also available free of charge via EDGAR through the SEC website at www.sec.gov. In addition, the public may read and copy materials filed by us with the SEC at the SEC's public reference room located at 100 F Street, NE, Washington, D.C., 20549. Information regarding operation of the SEC's public reference room can be obtained by calling the SEC at 1-800-732-0330.

ITEM 1A. RISK FACTORS

Before deciding to invest in our company, or to maintain or increase your investment, you should carefully consider the risks described below, in addition to the other information contained in this Annual Report on Form 10-K and other reports we have filed with the SEC. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us, or that we currently deem immaterial, may also affect our business operations. If any of these risks are realized, our business, financial condition, or results of operations could be seriously harmed and in that event, the market price for our common stock could decline, and you may lose all or part of your investment.

These risk factors should be considered in connection with evaluating the forward-looking statements contained in this Annual Report on Form 10-K. These factors could cause actual results and conditions to differ materially from those projected in our forward-looking statements.

Risks Related to Our Business

Our sales depend on coverage and reimbursement from third-party payers and a reduction in the coverage and/or reimbursement for our products could have a material adverse effect on our product sales, business and results of operations.

Sales of our products are dependent on the availability and extent of coverage and reimbursement, or level of reimbursement, from third-party payers, including government programs and private insurance plans. Governments and private payers may regulate prices, reimbursement levels and/or access to our products to contain costs or to affect levels of use. We rely in large part on the reimbursement of our products through government programs such as Medicare and Medicaid in the United States, and a reduction in the coverage and/or reimbursement for our products could have a material adverse effect on our product sales, business and results of operations.

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A substantial portion of our U.S. business relies on reimbursement from the U.S. federal government under Medicare Part B coverage. Most of our products furnished to Medicare beneficiaries in both a physician office setting and hospital outpatient setting are reimbursed under the Medicare Part B Average Sales Price, or ASP, payment methodology. ASP-based reimbursement of our products under Medicare may be below or could fall below the cost that some medical providers pay for such products, which could materially and adversely affect sales of our products. We also face risks relating to the reporting of pricing data that affect the U.S. reimbursement of and discounts for our products. ASP data are calculated by the manufacturer based on a formula defined by statute and regulation and are then submitted to the Centers for Medicare & Medicaid Services, or CMS, the agency responsible for administering the Medicare program, on a quarterly basis.

CMS uses those ASP data to determine the applicable reimbursement rates for our products under Medicare Part B. However, the statute, regulations and CMS guidance do not define specific methodologies for all aspects of the reporting of ASP data. For example, CMS has not provided specific guidance regarding administrative fees paid to group purchasing organizations, or GPOs, in the ASP calculation. CMS directs that manufacturers make “reasonable assumptions” in their calculation of ASP data in the absence of specific CMS guidance on a topic. As a result, we are required to apply our reasonable judgment to certain aspects of calculating ASP data. If our submitted ASP data are incorrect, we may become subject to substantial fines and penalties or other government enforcement actions, which could have a material adverse impact on our business and results of operations.

Clinical trials may fail to demonstrate the safety and efficacy of our drug products, which could prevent or significantly delay obtaining regulatory approval.

Prior to receiving approval to commercialize any of our drug products, we must demonstrate with substantial evidence from well-controlled clinical trials, and to the satisfaction of the FDA, and other regulatory authorities in the U.S. and other countries, that each of the products is both safe and effective. For each drug product, we will need to demonstrate its efficacy and monitor its safety throughout the process. If such development is unsuccessful, our business and reputation would be harmed and our stock price would be adversely affected.

All of our drug products are prone to the risks of failure inherent in drug development. Clinical trials of new drug products sufficient to obtain regulatory marketing approval are expensive, uncertain, and take years to complete. We may not be able to successfully complete clinical testing within the time frame we have planned, or at all. We may experience numerous unforeseen events during, or as a result of, the clinical trial process that could delay or prevent us from receiving regulatory approval or commercializing our drug products. In addition, the results of pre-clinical studies and early-stage clinical trials of our drug products do not necessarily predict the results of later-stage clinical trials. Later-stage clinical trials may fail to demonstrate that a drug product is safe and effective despite having progressed through initial clinical testing. Even if we believe the data collected from clinical trials of our drug products is promising, data are susceptible to varying interpretations, and such data may not be sufficient to support approval by the FDA or any other U.S. or foreign regulatory approval. Pre-clinical and clinical data can be interpreted in different ways.

Accordingly, FDA officials could interpret such data in different ways than we or our partners do which could delay, limit or prevent regulatory approval. The FDA, other regulatory authorities, our institutional review boards, our contract research organizations, or we may suspend or terminate our clinical trials for our drug products. Any failure or significant delay in completing clinical trials for our drug products, or in receiving regulatory approval for the sale of any drugs resulting from our drug products, may severely harm our business and reputation. Even if we receive FDA and other regulatory approvals, our drug products may later exhibit adverse effects that may limit or prevent their widespread use, may cause the FDA to revoke, suspend or limit their approval, or may force us to withdraw products derived from those drug products from the market.

Moreover, the commencement and completion of clinical trials may be delayed by many factors that are beyond our control, including:

- delays obtaining regulatory approval to commence a trial;
- reaching agreement on acceptable terms with contract research organizations, or CROs, and clinical trial sites;

- obtaining institutional review board, or IRB, approval at each site;
- slower than anticipated patient enrollment;
- scheduling conflicts with participating clinicians and clinical institutions;
- lack of funding;
- negative or inconclusive results;

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- patient noncompliance with the protocol;
- adverse medical events or side effects among patients during the clinical trials;
- negative or problematic FDA inspections of our clinical operations or manufacturing operations; and
- real or perceived lack of effectiveness or safety.

We could encounter delays if a clinical trial is suspended or terminated by us, the IRBs of the clinical trial sites in which such trials are being conducted, or by the FDA or other regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial.

Pricing for pharmaceutical products has come under increasing scrutiny by governments, legislative bodies and enforcement agencies. Changes in laws and regulations that control drug pricing for government programs may adversely impact our operating results and our business.

Many companies in our industry have received a governmental request for documents and information relating to drug pricing and patient support programs. We may become subject to similar requests, which would require us to incur significant expense and result in distraction for our management team. Additionally, to the extent there are findings, or even allegations, of improper conduct on the part of the company, such findings could further harm our business, reputation and/or prospects. It is possible that such inquiries could result in negative publicity or other negative actions that could harm our reputation; changes in our product pricing and distribution strategies; reduced demand for our approved products and/or reduced reimbursement of approved products, including by federal health care programs such as Medicare and Medicaid and state health care programs.

In addition, President Trump’s administration has indicated an interest in taking measures pertaining to drug pricing, including potential proposals relating to Medicare price negotiations, and importation of drugs from other countries. There have been several recent U.S. Congressional inquiries and proposed bills designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. At this time, it is unclear whether any of these proposals will be pursued and how they would impact our products or our future product candidates.

Our efforts to acquire or in-license and develop additional drug products may fail, which might limit our ability to grow our business.

To remain competitive and grow our business, our long-term strategy includes the acquisition or in-license of additional drug products. We are actively seeking to acquire, or in-license, additional commercial drug products as well as drug products that have demonstrated positive pre-clinical and/or clinical data. We have certain criteria that we are looking for in any drug product acquisition and in-license and we may not be successful in locating and acquiring, or in-licensing, additional desirable drug products on acceptable terms.

To accomplish our acquisition and in-license strategy, we intend to commit efforts, funds and other resources to research and development and business development. Even with acquired and in-licensed drug products, a high rate of failure is inherent in the development of such products. We must make ongoing substantial expenditures without any assurance that our efforts will be commercially successful. Failure can occur at any point in the process, including after significant funds have been invested. For example, promising new drug product candidates may fail to reach the market or may only have limited commercial success because of efficacy or safety concerns, failure to achieve positive clinical outcomes, inability to obtain necessary regulatory approvals, limited scope of approved uses, excessive costs to manufacture, the failure to establish or maintain intellectual property rights or infringement of the intellectual property rights of others.

In addition, many other large and small companies within the pharmaceutical and biotechnology industry seek to establish collaborative arrangements for product research and development, or otherwise acquire products in late-stage clinical development, in competition with us. We face additional competition from public and private research organizations, academic institutions and governmental agencies in establishing collaborative arrangements for drug products in late-stage clinical development. Many of the companies and institutions that compete against us have substantially greater capital resources, research and development staffs and facilities than we have, and greater experience in conducting business development activities. These entities represent significant competition to us as we seek to expand our portfolio through the in-license or

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acquisition of compounds. Finally, while it is not feasible to predict the actual cost of acquiring and developing additional drug products, that cost could be substantial and we may need to raise additional financing for such purpose, which may further dilute existing stockholders.

We are aware of several competitors attempting to develop and market products competitive to our products, which may reduce or eliminate our commercial opportunities.

The pharmaceutical and biotechnology industries are intensely competitive and subject to rapid and significant technological changes, and a number of companies are pursuing the development of pharmaceuticals and products that target the same diseases and conditions that our products target, including products currently commercialized. We cannot predict with accuracy the timing or impact of the introduction of potentially competitive products or their possible effect on our sales. Certain potentially competitive products to our products are in various stages of development, some of which have pending applications for approval with the FDA or have been approved by regulatory authorities in other countries. Also, there are many ongoing studies with currently marketed products and other developmental products, which may yield new data that could adversely impact the use of our products in their current and potential future indications. The introduction of competitive products could significantly reduce our sales, which, in turn would adversely impact our financial and operating results.

Reports of adverse events or safety concerns involving each of our products or similar agents, sold by us or our development partners and/or licensees, could delay or prevent us from obtaining or maintaining regulatory approval or negatively impact sales.

Certain of our products may cause SAEs. In addition to the risk associated with known SAEs, discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, could interrupt, delay or halt clinical trials of such products, including the FDA-required post-approval studies, and could result in the FDA or other regulatory authorities denying or withdrawing approval of our products for any or all indications. The FDA, other regulatory authorities or we may suspend or terminate clinical trials at any time. We may also be required to update the package inserts based on reports of adverse events or safety concerns or implement a risk evaluation and mitigation strategy, or REMS, which could adversely affect such product's acceptance in the market. In addition, the public perception of our products might be adversely affected, which could harm our business and results of operations and cause the market price of our common stock to decline, even if the concern relates to another company's product or product candidate. Our planned trials to demonstrate efficacy in a variety of indications and to better manage side effect profiles of certain of our products may not be successful.

The known SAEs related to our commercialized products are as follows:

FOLOTYN:

Forty-four percent of patients experienced a serious adverse event while on the study or within 30 days after their last dose. The most common serious adverse events (> 3%), regardless of causality, were fever, mucositis (redness and sores of the mucous membrane lining of the mouth, lips, throat, stomach, and genitals), sepsis (complication of infection), febrile neutropenia (fever associated with low white blood cell count), dehydration, dyspnea (shortness of breath), and thrombocytopenia (low platelet count). One death from cardiopulmonary arrest in a patient with mucositis and febrile neutropenia was reported in this trial. Deaths from mucositis, febrile neutropenia, sepsis, and pancytopenia (deficiency of all three cellular components of the blood) occurred in 1.2% of patients treated on all FOLOTYN trials at doses ranging from 30 to 325 mg/m2.

FOLOTYN may cause serious side effects, including bone marrow suppression, manifested by thrombocytopenia (low platelet counts), neutropenia (low white blood cell counts), and/or anemia (low red blood cell count); mucositis (redness and sores of the mucous membrane lining of the mouth, lips, throat, stomach, and genitals); dermatologic reactions (severe skin reactions); tumor lysis syndrome (tumor cells releasing contents into blood stream); hepatic toxicity (harm to liver); risk of increased toxicity in the presence of impaired renal function (increased harm to the patients with abnormal kidney function); and embryo-fetal toxicity (harm to an unborn baby).

ZEVALIN:

ZEVALIN is associated with the following serious adverse reactions: serious infusion reactions, prolonged and severe cytopenias (low blood cell count), cutaneous and mucocutaneous (skin and mucus membrane)

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reactions, and leukemia and myelodysplastic syndrome. The most serious adverse reactions of ZEVALIN are prolonged and severe cytopenias (low platelets, red blood cells, lymphocytes, white blood cells) and secondary malignancies.

MARQIBO:

Seventy-six percent of patients experienced serious adverse events during the studies. The most commonly reported serious adverse events (> 6%) included, febrile neutropenia (fever associated with low white blood cell count), fever, low-blood pressure, respiratory distress, and cardiac arrest.

MARQIBO may cause serious side effects, including extravasation tissue injury (leakage-induced tissue injury); neurologic toxicity (nerve problems, e.g., neuropathy); myelosuppression (low blood cell counts); tumor lysis syndrome (tumor cells releasing contents into blood stream); constipation and bowel obstruction (constipation and bowel blockage); fatigue (tiredness); hepatic toxicity (harm to liver); and embryo-fetal toxicity (harm to an unborn baby).

BELEODAQ:

Forty-seven percent of patients experienced serious adverse reactions while taking BELEODAQ or within 30 days after their last dose of BELEODAQ. The most common serious adverse reactions (> 2%) were pneumonia, fever, infection, anemia (low red blood cell count), increased creatinine, thrombocytopenia (low platelet count), and multi-organ failure. One treatment-related death associated with hepatic failure was reported in the trial.

BELEODAQ may cause serious side effects, including hematologic toxicity (low blood cell counts); serious infections; hepatotoxicity (liver problems); tumor lysis syndrome (tumor cell releasing contents into blood stream); gastrointestinal toxicity, including nausea, vomiting, and diarrhea; and embryo-fetal toxicity (harm to an unborn baby).

EVOMELA:

Twenty percent of patients experienced a treatment emergent serious adverse reaction while on study. The most common serious adverse reactions (>1 patient, 1.6%) were fever, hematochezia (blood in stools), febrile neutropenia (fever associated with low white blood cell count), and kidney failure. Treatment-related serious adverse reactions reported in >1 patient were pyrexia, febrile neutropenia, and hematochezia.

EVOMELA may cause serious side effects, including bone marrow suppression (low blood cell counts); gastrointestinal toxicity, including nausea, vomiting, diarrhea and mucositis (redness and sores of the lining of the mouth, lips, throat, stomach, and genitals); hepatotoxicity (liver problems); hypersensitivity (allergic reactions); secondary malignancies (secondary cancers); embryo-fetal toxicity (harm to an unborn baby); and infertility (harm to reproductive system).

Our supply of APIs, and drug products will be dependent upon the production capabilities of contract manufacturing organizations, or CMOs, component and packaging supply sources, other third-party suppliers, and other providers of logistical services, some of whom are based overseas and, if these parties are not able to meet our demands and FDA scrutiny, we may be limited in our ability to meet demand for our products, ensure regulatory compliance or maximize profit on the sale of our products.

We have no internal manufacturing capacity for APIs or our drug products, and, therefore, we have entered into agreements with CMOs and other suppliers to supply us with APIs and our finished dose drug products. Success in the

development and marketing of our drug products depends, in part, upon our ability to maintain, expand and enhance our existing relationships and establish new sources of supply. Some of the third-party manufacturing facilities used in the production of APIs and our drug products are located outside the U.S. The manufacture of APIs and finished drug products, including the acquisition of compounds used in the manufacture of the finished drug product, may require considerable lead times. We have little or no control over the production processes of third-party manufacturers, CMOs or other suppliers.

Our ability to source APIs and drug products is also dependent on providers of logistical services who may be subject to disruptions that we cannot predict or sufficiently plan around. Accordingly, while we do not currently anticipate shortages of supply, circumstances could arise in which we will not have adequate supplies to timely meet our requirements or market

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demand for a particular drug product could outstrip the ability of our supply source to timely manufacture and deliver the product, thereby causing us to lose sales. In addition, our ability to make a profit on the sale of our drug products depends on our ability to obtain price arrangements that ensure a supply of product at favorable prices.

If problems arise during the production of a batch of our drug products, that batch of product may have to be discarded. This could, among other things, lead to increased costs, lost revenue, damage to customer relations, time and expense spent investigating the cause and, depending on the cause, similar losses with respect to other batches or products. If problems are not discovered before the product is released to the market, recall and product liability costs may also be incurred. To the extent that one of our suppliers experiences significant manufacturing problems, this could have a material adverse effect on our revenues and profitability.

Finally, reliance on CMOs entails risks to which we would not be subject if we manufactured products ourselves, including reliance on the third party for regulatory compliance and adherence to the cGMP, requirements, the possible breach of the manufacturing agreement by the CMO and the possibility of termination or non-renewal of the agreement by the CMO, based on its own business priorities, at a time that is costly or inconvenient for us. Before we can obtain marketing approval for our drug products, our CMO facilities must pass an FDA pre-approval inspection. In order to obtain approval, all of the facility's manufacturing methods, equipment and processes must comply with cGMP requirements.

The cGMP requirements govern all areas of record keeping, production processes and controls, personnel and quality control. In addition, our CMOs will be subject to on-going periodic inspection by the FDA and corresponding state and foreign agencies for compliance with cGMP regulations, similar foreign regulations and other regulatory standards. We do not have control over our CMOs' compliance with these regulations and standards. Any failure of our third party manufacturers or us to comply with applicable regulations, including an FDA pre-approval inspection and cGMP requirements, could result in sanctions being imposed on them or us, including warning letters, fines, injunctions, civil penalties, failure of regulatory authorities to grant marketing approval of our products, delay, suspension or withdrawal of approvals, license revocation, seizures or recalls of product, operation restrictions and criminal prosecutions, any of which could significantly and adversely affect our business.

Servicing our debt requires a significant amount of cash, and we may not have sufficient cash flow from our business to pay our substantial debt.

As of December 31, 2016, we owed $110 million of principal from our December 2013 issuance of convertible notes, which mature in December 2018. Any such indebtedness will require the dedication of a portion of our expected cash flow from operations to service our indebtedness, thereby reducing the amount of our cash flow available for other purposes. In addition, our ability to make scheduled payments of the principal, to pay interest on or to refinance our indebtedness, including our convertible notes, depends on our future performance, which is subject to regulatory, economic, financial, competitive and other factors beyond our control, and our ability to raise equity capital.

Our business may not continue to generate cash flow from operations in the future sufficient to service our debt and make necessary capital expenditures. If we are unable to generate such cash flow, we may be required to adopt one or more alternatives, such as selling assets, restructuring debt or obtaining additional equity capital on terms that may be onerous or highly dilutive. Our ability to refinance our indebtedness will depend on the capital markets and our financial condition at such time. We may not be able to engage in any of these activities or engage in these activities on desirable terms, which could result in a default on our debt obligations.

Wholesaler actions could increase competitive and pricing pressures on pharmaceutical manufacturers, including us.

We sell certain of our products primarily through wholesalers, who in turn sell to end-users. These wholesalers comprise a significant part of the distribution network for pharmaceutical products in the U.S. A small number of large wholesalers control a significant share of the market, which can increase competitive and pricing pressures on pharmaceutical manufacturers, including us. In addition, wholesalers may apply pricing pressure through their fee-for-service arrangements.

Our dependence on key executives, scientists and sales and marketing personnel could impact the development and management of our business.

We are highly dependent upon our ability to attract and retain qualified scientific, technical sales and marketing and managerial personnel. There is intense competition for qualified personnel in the pharmaceutical and biotechnology industries, and we cannot be sure that we will be able to continue to attract and retain the qualified personnel necessary, particularly as

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business prospects change, for the development and management of our business. Although we do not believe the loss of one individual would materially harm our business, our business might be harmed by the loss of the services of multiple existing personnel, as well as the failure to recruit additional key scientific, technical and managerial personnel in a timely manner. Much of the know-how we have developed resides in our scientific and technical personnel and is not readily transferable to other personnel. While we have an employment agreement with our Chief Executive Officer, we do not have employment agreements with any of our other key scientific, technical, or managerial employees.

If the distributors that we rely upon to sell our products fail to perform, our business may be adversely affected.

Our success depends on the continued customer support efforts of our network of distributors. In the U.S., we sell our products to a small number of distributors who in turn sell-through to patient health care providers. These distributors also provide multiple logistics services relating to the distribution of our products, including transportation, warehousing, cross-docking, inventory management, packaging and freight-forwarding. We do not promote products to these distributors and they do not set or determine demand for products. The use of distributors involves certain risks, including, but not limited to, risks that these distributors will:

- not provide us with accurate or timely information regarding their inventories, the number of patients who are using our products or complaints about our products;
- not purchase sufficient inventory on hand to fulfill end user orders in a timely manner;
- be unable to satisfy financial obligations to us or others; and
- cease operations.

Any such actions may result in decreased sales of our products, which would harm our business.

Adverse economic conditions may have material adverse consequences on our business, results of operations and financial condition.

Unpredictable and unstable changes in economic conditions, including recession, inflation, increased government intervention, or other changes, may adversely affect our general business strategy. We rely upon our ability to generate positive cash flow from operations to fund our business. If we are not able to generate positive cash flow from operations, we may need to utilize sources of financing or other sources of cash. We may need to raise additional funds through public or private debt or equity financings in order to fund existing operations or to take advantage of opportunities, including acquisitions of complementary businesses or technologies. In addition, if our business deteriorates, we may not be able to maintain compliance with any covenants or representations and warranties in any such financings which could result in reduced availability of such financings, an event of default under such financings, or could make other sources of financing unavailable to us. Any such event would have a material adverse impact on our business, results of operations and financial condition.

While we believe we have adequate capital resources to meet current working capital and capital expenditure requirements, an economic downturn or an increase in our expenses could require additional financing on less than attractive rates or on terms that are excessively dilutive to existing stockholders. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and stock price and could require us to delay or abandon clinical development plans or plans to acquire additional technology.

Volatile economic conditions may not only limit our access to capital, but may also make it difficult for our customers and us to accurately forecast and plan future business activities, and they could cause businesses to slow spending on our products, which would delay and lengthen sales cycles. Furthermore, during challenging economic times, our customers may face issues gaining timely access to sufficient credit, which could result in an impairment of their ability to make timely payments to us. In addition, adverse economic conditions could also adversely impact our suppliers' ability to provide us with materials which would negatively impact on our business, financial condition, and results of operations.

We are a small company relative to our principal competitors, and our limited financial resources may limit our ability to develop and market our drug products.

Many companies, both public and private, including well-known pharmaceutical companies and smaller niche-focused companies, are developing products to treat many, if not all, of the diseases we are pursuing or are currently distributing drug products that directly compete with the drugs that we sell or that we intend to develop, market and distribute. Many of these

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companies have substantially greater financial, research and development, manufacturing, marketing and sales experience and resources than us. As a result, our competitors may be more successful than us in developing their products, obtaining regulatory approvals and marketing their products to consumers.

Competition for branded or proprietary drugs is less driven by price and is more focused on innovation in the treatment of disease, advanced drug delivery and specific clinical benefits over competitive drug therapies. We may not be successful in any or all of our current clinical studies; or if successful, and if one or more of our drug products is approved by the FDA, we may encounter direct competition from other companies who may be developing products for similar or the same indications as our drug products.

Companies that have products on the market or in research and development that target the same indications as our products include, among others, AstraZeneca plc, Bayer AG, Endo International plc, Eli Lilly and Company, Novartis International AG, Genentech, Inc. (Roche Holding AG), Bristol-Myers Squibb Company, Seattle Genetics, Inc., GlaxoSmithKline plc, Biogen Inc., OSI Pharmaceuticals, Inc. (Astellas Pharma Inc.), Cephalon, Inc. (Teva Pharmaceutical Industries Ltd.), Sanofi S.A., Pfizer, Inc., Merck & Company Inc., Celgene Corporation, BiPar Sciences, Inc. (Sanofi S.A.), Sanofi Genzyme, Shire plc, AbbVie Inc., Poniard Pharmaceuticals, Inc., and Johnson & Johnson. These companies may be more advanced in the development of competing drug products or are more established.

Many of our competitors are large and well-capitalized companies focusing on a wide range of diseases and drug indications, and have substantially greater financial, research and development, marketing, human and other resources than we do. Furthermore, large pharmaceutical companies have significantly more experience than we do in pre-clinical testing, human clinical trials and regulatory approval procedures, among other things.

Because we have obtained accelerated approval to market FOLOTYN, BELEODAQ and MARQIBO, we are subject to ongoing regulatory obligations and review, including completion of the post-approval requirements.

FOLOTYN and BELEODAQ were approved for the treatment of patients with relapsed or refractory PTCL, and MARQIBO was approved for the treatment of adult patients with Philadelphia chromosome-negative ALL in second or greater relapse or whose disease has progressed following two or more anti-leukemia therapies, under the FDA's accelerated approval regulations. These provisions allow the FDA to approve products for cancer or other serious or life threatening diseases based on initial positive data from clinical trials. Under these provisions, we are subject to certain post-approval requirements. Specifically, we are required to conduct Phase 1 dose escalating studies and a Phase 3 randomized study for FOLOTYN and BELEODAQ in patients with PTCL. The FDA also required that we conduct two Phase 1 trials to assess whether FOLOTYN poses a serious risk of altered drug levels resulting from organ impairment as well as additional post-marketing studies with BELEODAQ. For MARQIBO, we are required to conduct a randomized Phase 3 study in patients over 60 years of age with newly diagnosed ALL. Failure to complete the studies or adhere to the timelines established by the FDA could result in penalties, including fines or withdrawal of FOLOTYN, BELEODAQ, and/or MARQIBO from the market.

The FDA may also initiate proceedings to withdraw approval or request that we voluntarily withdraw these drugs from the market if our Phase 3 studies fail to confirm clinical benefit. Further, the FDA may require us to amend the package inserts for these drugs, including by strengthening the warnings and precautions section or institute a REMS based on the results of these studies or clinical experience. We are also subject to additional, continuing post-approval regulatory obligations, including the possibility of additional clinical studies required by the FDA, safety reporting requirements and regulatory oversight of the promotion and marketing of these drugs.

We and our third-party contract manufacturers are subject to inspection by regulatory authorities.

We and our third-party manufacturers are required to adhere to cGMP. The cGMP regulations cover all aspects of the manufacturing, storage, testing, quality control and record keeping relating to our drugs.

We and or our third-party contract manufacturers are subject to periodic inspection by the FDA and foreign regulatory authorities to ensure compliance with cGMP or other applicable government regulations and corresponding foreign standards. We have limited control over a third-party manufacturer's compliance with these regulations and standards. If we or our third-party manufacturers fail to comply with applicable regulatory requirements, we may be subject to fines, suspension, modification or withdrawal of regulatory approvals, product recalls, seizure of products, operating

restrictions and criminal prosecution.

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If actual future payments for allowances for discounts, returns, rebates and chargebacks exceed the estimates we made at the time of the sale of our products, including, without limitation, due to a change in the composition of our sales over time, our financial position, results of operations and cash flows may be materially and negatively impacted.

We recognize product revenue net of estimated allowances for discounts, returns, rebates and chargebacks. Such estimates require our most subjective and complex judgment due to the need to make estimates about matters that are inherently uncertain. Based on industry practice, pharmaceutical companies, including us, have liberal return policies. Our FUSILEV, MARQIBO, and BELEODAQ customers are permitted to return purchased products beginning at its expiration date and within six months thereafter. Our EVOMELA customers are permitted to return purchased product beginning at six months prior to its expiration date, and within 12 months following its expiration date (as well as for overstock inventory, as determined by end-users). We authorize returns for damaged products and exchanges for expired products in accordance with our return goods policy and procedures. Also, like our competitors, we also give credits for chargebacks to wholesale customers that have contracts with us for their sales to hospitals, group purchasing organizations, pharmacies or other retail customers.

A chargeback is the difference between the price the wholesale customer (in our case, the GPOs) pays (wholesale acquisition cost) and the price that the GPO's end-customer pays for a product (contracted customer). For instance, our products are subject to certain programs with federal government qualified entities whereby pricing on products is discounted to such entities and results in a chargeback claim to us. To the extent that our sales to discount purchasers, such as federal government qualified entities, increases, our chargebacks will also increase. There may be significant lag time between our original sale to the wholesaler and our receipt of the corresponding government chargeback claims from our wholesalers.

Our products are subject to state government-managed Medicaid programs, whereby rebates for purchases are issued to participating state governments. These rebates arise when the patient treated with our products is covered under Medicaid. Our calculations related to these Medicaid rebate accruals require us to estimate end-user and patient mix to determine which of our sales will likely be subject to these rebates. There is a significant time lag in us receiving these rebate notices (generally several months after our sale is made). Our estimates are based on our historical claims from participating state governments, as supplemented by management's judgment.

Although we believe that we have sufficient allowances, actual results may differ significantly from our estimated allowances for discounts, returns, rebates and chargebacks. Changes in estimates and assumptions based upon actual results may have a material impact on our financial condition, results of operations and cash flows. Such changes to estimates will be made to the financial statements in the year in which the estimate is changed. In addition, our financial position, results of operations and cash flows may be materially and negatively impacted if actual future payments for allowances, discounts, returns, rebates and chargebacks exceed the estimates we made at the time of the sale of our products.

The marketing and sale of our products may be adversely affected by the marketing and sales efforts of third parties who sell our products or similar products outside of our territories.

We have only licensed the rights to develop and market our products in limited territories. Other companies market and sell the same products in other parts of the world. If, as a result of other companies' actions, negative publicity is associated with our products or similar products, our own efforts to successfully market and sell our products in our markets may be adversely impacted.

We may not be able to successfully integrate our acquisitions and any additional businesses we may acquire.

We regularly evaluate and, as appropriate, may make selective acquisitions of businesses and intellectual property that we believe complement or augment our existing business. Issues that could delay or prevent integration of the acquired business and/or intellectual property into our own include:

- conforming standards, procedures and policies, business cultures and compensation structures;
- conforming information technology and accounting systems;
- consolidating corporate and administrative infrastructures;
- consolidating sales and marketing operations;

- retaining existing customers and attracting new customers;
- retaining key employees;

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- identifying and eliminating redundant and under-performing operations and assets;
- minimizing the diversion of management's attention from ongoing business concerns;
- coordinating geographically dispersed organizations;
- managing tax costs or inefficiencies associated with integrating operations; and
- making any necessary modifications to operating control standards to comply with the Sarbanes-Oxley Act of 2002 and the rules and regulations promulgated thereunder.

If we are unable to successfully integrate our acquisitions with our existing business, we may not obtain the advantages that the acquisitions were intended to create, which may materially adversely affect our business, results of operations, financial condition and cash flows, our ability to develop and introduce new products and the market price of our stock. Actual costs and sales synergies, if achieved at all, may be lower than we expect and may take longer to achieve than we anticipate. Furthermore, the products of companies we acquire may overlap with our products or those of our customers, creating conflicts with existing relationships or with other commitments that are detrimental to the integrated businesses.

Our collaborations with outside scientists may be subject to change, which could limit our access to their expertise.

We work with scientific advisors and collaborators at research institutions. These scientists are not our employees and may have other commitments that would limit their availability to us. If a conflict of interest between their work for us and their work for another entity arises, we may lose their services, which could negatively impact our research and development activities.

We may rely on contract research organizations, or CROs, and other third parties to conduct clinical trials and, in such cases, we are unable to directly control the timing, conduct and expense of our clinical trials.

We may rely, in full or in part, on third parties to conduct our clinical trials. In such situations, we have less control over the conduct of our clinical trials, the timing and completion of the trials, the required reporting of adverse events and the management of data developed through the trial than would be the case if we were relying entirely upon our own staff. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. Outside parties may have staffing difficulties, may undergo changes in priorities or may become financially distressed, adversely affecting their willingness or ability to conduct our trials. We may experience unexpected cost increases that are beyond our control. Problems with the timeliness or quality of the work of a CRO may lead us to seek to terminate the relationship and use an alternative service provider. However, making this change may be costly and may delay our trials, and contractual restrictions may make such a change difficult or impossible. Additionally, it may be impossible to find a replacement organization that can conduct our trials in an acceptable manner and at an acceptable cost.

We may have conflicts with our third-party development partners that could delay or prevent the development or commercialization of our drug products.

We may have conflicts with our third-party development partners, such as conflicts concerning the interpretation of pre-clinical or clinical data, the achievement of milestones, the interpretation of contractual obligations, payments for services, development obligations or the ownership of intellectual property developed during our collaboration. If any conflicts arise with any of our third-party development partners, such partner may act in a manner that is adverse to our best interests. Any such disagreement could result in one or more of the following, each of which could delay or prevent the development or commercialization of our drug product, and in turn prevent us from generating revenues from such drug product:

- unwillingness on the part of a third-party development partner to pay us milestone payments or royalties that we believe are due to us under a collaboration;
- uncertainty regarding ownership of intellectual property rights arising from our collaborative activities, which could prevent us from entering into additional collaborations;

- unwillingness to cooperate in the manufacture of the product, including providing us with product data or materials;
- unwillingness to keep us informed regarding the progress of its development and commercialization activities or to permit public disclosure of the results of those activities;
- initiation of litigation or alternative dispute resolution options by either party to resolve the dispute;

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- attempts by either party to terminate the collaboration;
- our ability to maintain or defend our intellectual property rights may be compromised by our partner's acts or omissions;
- a third-party development partner may utilize our intellectual property rights in such a way as to invite litigation that could jeopardize or invalidate our intellectual property rights or expose us to potential liability;
- a third-party development partner may change the focus of its development and commercialization efforts due to internal reorganizations, mergers, consolidations and otherwise;
- unwillingness to fully fund or commit sufficient resources to the testing, marketing, distribution or development of our products;
- unwillingness or inability to fulfill their obligations to us due to the pursuit of alternative products, conflicts of interest that arise or changes in business strategy or other business issues; and/or
- we may not be able to guarantee supplies of development or marketed products.

Given these risks, it is possible that any collaborative arrangements which we have or could enter into may not be successful.

From time to time we may need to in-license patents and proprietary technologies from third parties, which may be difficult or expensive to obtain.

We may need to obtain licenses to patents and other proprietary rights held by third parties to successfully develop, manufacture and market our drug products. As an example, it may be necessary to use a third party's proprietary technology to reformulate one of our drug products in order to improve upon the capabilities of the drug product. If we are unable to timely obtain these licenses on reasonable terms, or at all, our ability to commercially exploit our drug products may be inhibited or prevented.

The potential size of the market for our drug products is uncertain.

We often provide estimates of the number of people who suffer from the diseases that our drugs are targeting. However, there is limited information available regarding the actual size of these patient populations. In addition, it is uncertain whether the results from previous or future clinical trials of drug products will be observed in broader patient populations, and the number of patients who may benefit from our drug products may be significantly smaller than the estimated patient populations.

Generic levo-leucovorin product competition could further adversely affect our FUSILEV revenues.

FUSILEV continues to face direct competition from generic levo-leucovorin products as a result of the FDA ANDA approval and competitive product launches by two companies in 2015. As a result, this generic competition is expected to continue to adversely impact our FUSILEV product value including (i) sales, demand and market share, (ii) the price we are able to charge, (iii) the inventory levels that wholesalers maintain, and (iv) product return rates. Additional companies are expected to launch their generic levo-leucovorin products in the future, which could further adversely impact FUSILEV revenues.

On April 27, 2015, we filed suit in the U.S. District Court for the District of Columbia against the FDA seeking a temporary restraining order or preliminary injunction to suspend FDA approval of Sandoz's ANDA. We have contended that Sandoz's ANDA should not have been approved until the expiry of our Orphan Drug Exclusivity on April 29, 2018. On April 29, 2015, the court denied the temporary restraining order and on May 27, 2015, the court entered summary judgment in favor of the FDA et al. On June 5, 2015, we filed our Notice of Appeal. On June 3, 2016, the U.S. Court of Appeals for the District of Columbia affirmed the judgment in favor of the FDA et al. All costs pertaining to this matter (incurred and accrued) have been recognized within "selling, general and administrative" expenses on the accompanying Consolidated Statements of Operations for all periods presented.

Our collaboration partner, Mundipharma, may not be successful in obtaining regulatory approval for FOLOTYN in a number of countries and FOLOTYN is subject to numerous complex regulatory requirements.

Our collaboration partner, Mundipharma, may not be successful in obtaining regulatory approval for FOLOTYN in a number of countries and FOLOTYN is subject to numerous complex regulatory requirements. Failure to comply with, or

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changes to, the regulatory requirements that are applicable to FOLOTYN outside the United States may result in a variety of consequences, including the following:

- restrictions on FOLOTYN or our manufacturing processes;
- warning letters;
- withdrawal of FOLOTYN from the market;
- voluntary or mandatory recall of FOLOTYN;
- fines against us;
- suspension or withdrawal of regulatory approvals for FOLOTYN;
- suspension or termination of any of our ongoing clinical trials of FOLOTYN;
- refusal to permit import or export of FOLOTYN;
- refusal to approve pending applications or supplements to approved applications that we submit;
- denial of permission to file an application or supplement in a jurisdiction;
- product seizure;
- and/or
- injunctions, consent decrees, or the imposition of civil or criminal penalties against us.

Changes in our effective income tax rate could adversely affect our profitability.

We are subject to federal and state income taxes in the U.S. and our tax liabilities are dependent upon the distribution of income among these different jurisdictions. Various factors may have favorable or unfavorable effects on our effective income tax rate. These factors include, but are not limited to:

- interpretations of existing tax laws;
- the accounting for stock options and other share-based compensation;
- changes in tax laws and rates;
- future levels of research and development spending;
- changes in accounting standards;
- changes in the mix of earnings in the various tax jurisdictions in which we operate;
- the outcome of examinations by the Internal Revenue Service and other jurisdictions;
- the accuracy of our estimates for unrecognized tax benefits;
- realization of deferred tax assets; and
- changes in overall levels of pre-tax earnings.

The impact on our income tax provision resulting from the above-mentioned factors may be significant and could have an impact on our profitability.

Earthquakes or other natural or man-made disasters and business interruptions could adversely affect our business.

Our operations are vulnerable to interruption by fire, power loss, floods, telecommunications failure and other events beyond our control. In addition, our operations are susceptible to disruption as a result of natural disasters such as earthquakes. So far we have never experienced any significant disruption of our operations as a result of earthquakes or other natural or man-made disasters. Although we have a contingency recovery plan, any significant business interruption could cause delays in our drug development and future sales and harm our business.

A breakdown or breach of our information technology systems and cyber security efforts could subject us to liability, reputational damage or interrupt the operation of our business.

We rely upon our sophisticated information technology systems and infrastructure to operate our business. In the ordinary course of business, we collect, store and transmit large amounts of confidential information (including, but not limited to, personal

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information and intellectual property), and we deploy and operate an array of technical and procedural controls to maintain the confidentiality and integrity of such confidential information. Data privacy breaches by those who access our systems may pose a risk that sensitive data, including intellectual property, trade secrets or personal information belonging to us, our patients, employees, customers or other business partners, may be exposed to unauthorized persons or to the public. We could also experience a business interruption, noncompliance with data privacy laws, theft of confidential information, or reputational damage from industrial espionage attacks, malware or other cyber-attacks, which may compromise our system infrastructure or lead to data leakage, either internally or at our third-party providers. Such attacks are of ever-increasing levels of sophistication, frequently and intensity, and have become increasingly difficult to detect. There can be no assurance that our efforts to protect our data and information technology systems will prevent breakdowns or breaches in our systems (or that of our third-party providers). Any such interruption or breach of our systems could adversely affect our business operations and/or result in the loss of critical or sensitive confidential information or intellectual property, and could result in financial, legal, business and reputational harm to us.

Risks Related to Our Industry

If we are unable to adequately protect our technology or enforce our patent rights, our business could suffer.

Our success with the drug products that we develop will depend, in part, on our ability and the ability of our licensors to obtain and maintain patent protection for these products. We currently have a number of U.S. and foreign patents issued and pending, however, we primarily rely on patent rights licensed from others. Our license agreements generally give us the right and/or obligation to maintain and enforce the subject patents. We may not receive patents for any of our pending patent applications or any patent applications we may file in the future. If our pending and future patent applications are not allowed or, if allowed and issued into patents, if such patents and the patents we have licensed are not upheld in a court of law, our ability to competitively exploit our drug products would be substantially harmed. Also, such patents may or may not provide competitive advantages for their respective products or they may be challenged or circumvented by our competitors, in which case our ability to commercially exploit these products may be diminished.

The patent positions of pharmaceutical and biotechnology companies can be highly uncertain and involve complex legal and factual questions. No consistent policy regarding the breadth of claims allowed in pharmaceutical and biotechnology patents has emerged to date in the U.S. The laws of many countries may not protect intellectual property rights to the same extent as U.S. laws, and those countries may lack adequate rules and procedures for defending our intellectual property rights. Filing, prosecuting and defending patents on all our products or product candidates throughout the world would be prohibitively expensive. Competitors may use our technologies in jurisdictions and may not be covered by any of our patent claims or other intellectual property rights.

Changes in either patent laws or in interpretations of patent laws in the U.S. and other countries may diminish the value of our intellectual property. We do not know whether any of our patent applications will result in the issuance of any patents, and we cannot predict the breadth of claims that may be allowed in our patent applications or in the patent applications we license from others.

The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- in certain jurisdictions, we or our licensors might not have been the first to make the inventions covered by each of our or our licensors' pending patent applications and issued patents, and we may have to participate in expensive and protracted interference proceedings to determine priority of invention;
- we or our licensors might not have been the first to file patent applications for these inventions;
- others may independently develop similar or alternative product candidates or duplicate any of our or our licensors' product candidates;
- our or our licensors' pending patent applications may not result in issued patents;
-

our or our licensors' issued patents may not provide a basis for commercially viable products or may not provide us with any competitive advantages or may be challenged by third parties;

- others may design around our or our licensors' patent claims to produce competitive products that fall outside the scope of our or our licensors' patents;
- we may not develop or in-license additional patentable proprietary technologies related to our product candidates; or

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- the patents of others may prevent us from marketing one or more of our product candidates for one or more indications that may be valuable to our business strategy.

An issued patent does not guarantee us the right to practice the patented technology or commercialize the patented product. Third parties may have blocking patents that could be used to prevent us from commercializing our patented products and practicing our patented technology. Our issued patents and those that may be issued in the future may be challenged, invalidated or circumvented, which could limit our ability to prevent competitors from marketing related product candidates or could limit the length of the term of patent protection of our product candidates. Our competitors may independently develop similar technologies. In addition, because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that, before any of our product candidates can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby reducing any advantage of the patent.

We also rely on trade secret protection and contractual protections for our unpatented and proprietary drug compounds. Trade secrets are difficult to protect. While we enter into confidentiality agreements with our employees, consultants and others, these agreements may not successfully protect our trade secrets or other confidential and proprietary information. It is possible that these agreements will be breached, or that they will not be enforceable in every instance, and that we will not have adequate remedies for any such breach. Likewise, although we conduct periodic trade secret audits of certain partners, vendors and contract manufacturers, these trade secret audits may not protect our trade secrets or other confidential and proprietary information. It is possible that despite having certain trade secret audited security measures in place, trade secrets or other confidential and proprietary information may still be leaked or disclosed to a third party. It is also possible that our trade secrets will become known or independently developed by our competitors.

We also rely on trademarks to protect the names of our products. These trademarks may be challenged by others. If we enforce our trademarks against third parties, such enforcement proceedings may be expensive. Some of our trademarks, including ZEVALIN are owned by, or assignable to, our licensors and, upon expiration or termination of the applicable license agreements, we may no longer be able to use these trademarks. If we are unable to adequately protect our technology, trade secrets or proprietary know-how, or enforce our patents and trademarks, our business, financial condition and prospects could suffer.

Intellectual property rights are complex and uncertain and therefore may subject us to infringement claims.

The patent positions related to our drug products are inherently uncertain and involve complex legal and factual issues. We believe that there is significant litigation in the pharmaceutical and biotechnology industry regarding patent and other intellectual property rights. A patent does not provide the patent holder with freedom to operate in a way that infringes the patent rights of others. We may be accused of patent infringement at any time. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. If we are sued for patent infringement, we would need to demonstrate that our products or methods do not infringe the patent claims of the relevant patent and/or that the patent claims are invalid or unenforceable, and we may not be able to do this. Proving invalidity, in particular, is difficult since it requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents in the U.S.

Although we are not aware of any infringement by any of our drug products on the rights of any third party, there may be third party patents or other intellectual property rights, including trademarks and copyrights, relevant to our drug products of which we are not aware. Third parties may assert patent or other intellectual property infringement claims against us, or our licensors and collaborators, with products. Any claims that might be brought against us relating to infringement of patents may cause us to incur significant expenses and, if successfully asserted against us, may cause us to pay substantial damages and result in the loss of our use of the intellectual property that is critical to our business strategy.

In the event that we or our partners are found to infringe any valid claim of a patent held by a third party, we may, among other things, be required to:

- pay damages, including up to treble damages and the other party’s attorneys’ fees, which may be substantial;

- cease the development, manufacture, use and sale of our products that infringe the patent rights of others through a court-imposed sanction such as an injunction;
- expend significant resources to redesign our products so they do not infringe others' patent rights, which may not be possible;
- discontinue manufacturing or other processes incorporating infringing technology; or
- obtain licenses to the infringed intellectual property, which may not be available to us on acceptable terms, or at all.

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Rapid bio-technological advancement may render our drug products obsolete before we are able to recover expenses incurred in connection with their development. As a result, some of our drug products may never become profitable.
The pharmaceutical industry is characterized by rapidly evolving biotechnology. Biotechnologies under development by other pharmaceutical companies could result in treatments for diseases and disorders for which we are developing our own treatments. Several other companies are engaged in research and development of compounds that are similar to our research. A competitor could develop a new biotechnology, product or therapy that has better efficacy, a more favorable side-effect profile or is more cost-effective than one or more of our drug products and thereby cause our drug products to become commercially obsolete. Some of our drug products may become obsolete before we recover the expenses incurred in their development. As a result, such products may never become profitable.
Failure to obtain regulatory approval outside the U.S. will prevent us from marketing our product candidates abroad.
We intend to market certain of our existing and future product candidates in and outside of the U.S. In order to market our existing and future product candidates in the EU and many other foreign jurisdictions, we must obtain separate regulatory approvals according to the applicable domestic laws and regulations. We have had limited interactions with foreign regulatory authorities, and the approval procedures vary among countries and can involve additional testing, and the time required to obtain approval may differ from that required to obtain FDA approval. Approval by the FDA does not guarantee approval by regulatory authorities in other countries, and approval by one or more foreign regulatory authorities does not necessarily ensure approval by regulatory authorities in other countries or by the FDA.

A failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory approval process in others. The foreign regulatory approval process may include all of the risks associated with obtaining FDA approval as well as other risks specific to the jurisdictions in which we may seek approval. We may not obtain foreign regulatory approvals on a timely basis, if at all. We may not be able to file for foreign regulatory approvals and may not receive necessary approvals to commercialize our existing and future product candidates in any market.
Competition for patients in conducting clinical trials may prevent or delay product development and strain our limited financial resources.
Many pharmaceutical companies are conducting clinical trials involving patients with the disease indications that our drug products target. As a result, we must compete with them for clinical sites, physicians and the limited number of patients who fulfill the stringent requirements for participation in clinical trials. Also, due to the confidential nature of clinical trials, we do not know how many of the eligible patients may be enrolled in competing studies and who are consequently not available to us for our clinical trials. Our clinical trials may be delayed or terminated due to the inability to enroll enough patients. Patient enrollment depends on many factors, including the size of the patient population, the nature of the trial protocol, the proximity of patients to clinical sites and the eligibility criteria for the study. The delay or inability to meet planned patient enrollment may result in increased costs and delays or termination of the trial, which could have a harmful effect on our ability to develop products.
Even after we receive regulatory approval to market our drug products, the market may not be receptive to our drug products upon their commercial introduction, which would negatively impact our ability to achieve profitability.
Our drug products may not gain market acceptance among physicians, patients, healthcare payers and the medical community. The degree of market acceptance of any approved drug products will depend on a number of factors, including:

- the effectiveness of the drug product;
- the prevalence and severity of any side effects;
- potential advantages or disadvantages over alternative treatments;
- relative convenience and ease of administration;
- the strength of marketing and distribution support;
- the price of the drug product, both in absolute terms and relative to alternative treatments; and
- sufficient third-party coverage and reimbursement.

If our drug products receive regulatory approval but do not achieve an adequate level of acceptance by physicians, healthcare payers and patients, we may not generate drug product revenues sufficient to attain profitability.

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Guidelines and recommendations published by various organizations can reduce the use of our products.
Government agencies, such as the CMS, promulgate regulations, and issue guidelines, directly applicable to us and to our products. In addition, third parties such as professional societies, practice management groups, insurance carriers, physicians, private health/science foundations and organizations involved in various diseases from time to time may publish guidelines or recommendations to healthcare providers, administrators and payers, and patient communities. Recommendations may relate to such matters as utilization, dosage, route of administration and use of related therapies and coverage and reimbursement of our products by government and private payers. Third-party organizations like the above have in the past made recommendations about our products. Recommendations or guidelines that are followed by patients and healthcare providers could result in decreased utilization and/or dosage of our products, any of which could adversely affect our product sales and operating results materially.
The sale of our products is subject to regulatory approvals, and our business is subject to extensive regulatory requirements, and if we are unable to obtain regulatory approval for our product candidates, or if we fail to comply with governmental regulations we will be limited in our ability to commercialize our products and product candidates and/or subject us to penalties.
We are not permitted to market or promote any of our product candidates before we receive regulatory approval from the FDA or comparable foreign regulatory authorities, and we may never receive such regulatory approval for any of our product candidates. Obtaining regulatory approval of a new drug is an uncertain, lengthy and expensive process, and success is never guaranteed. Despite the time, resources and effort expended, failure can occur at any stage. In order to receive approval from the FDA for each product candidate, we must demonstrate that the new drug product is safe and effective for its intended use and that the manufacturing processes for the product candidate comply with the FDA's cGMPs. cGMPs include requirements related to production processes, quality control and assurance, and recordkeeping. The FDA has substantial discretion in the approval process for human medicines.

The FDA and comparable agencies in foreign countries impose many requirements related to the drug development process through lengthy and rigorous clinical testing and data collection procedures, and other costly and time consuming compliance procedures. While we believe that we are currently in compliance with applicable FDA regulations, if our partners, the CROs or CMOs with which we have relationships, or we fail to comply with the regulations applicable to our clinical testing, the FDA may delay, suspend or cancel our clinical trials, or the FDA might not accept the test results. The FDA, an institutional review board, third party investigators, any comparable regulatory agency in another country, or we, may suspend clinical trials at any time if the trials expose subjects participating in such trials to unacceptable health risks. Further, human clinical testing may not show any current or future drug product to be safe and effective to the satisfaction of the FDA or comparable regulatory agencies, or the data derived from the clinical tests may be unsuitable for submission to the FDA or other regulatory agencies. Once we submit an application seeking approval to market a drug product, the FDA or other regulatory agencies may not issue their approvals on a timely basis, if at all. If we are delayed or fail to obtain these approvals, our business and prospects may be significantly damaged. In addition, any regulatory approvals that we receive for our future product candidates may also be subject to limitations on the indicated uses for which they may be marketed or contain requirements for potentially costly post-marketing follow-up studies and surveillance to monitor the safety and efficacy of the product.
If we obtain regulatory approval for our drug products, we, our partners, our manufacturers, and other contract entities will continue to be subject to extensive requirements by a number of national, foreign, state and local agencies. These regulations will impact many aspects of our operations, including testing, research and development, manufacturing, safety, effectiveness, labeling, storage, quality control, adverse event reporting, record keeping, approval, advertising and promotion of our future products. The FDA and foreign regulatory authorities strictly regulate the promotional claims that may be made about prescription products and our product labeling, advertising and promotion is subject to continuing regulatory review. Physicians may nevertheless prescribe our product to their patients in a manner that is inconsistent with the approved label, or that is off-label. The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and if we are found to have improperly promoted

off-label uses we may be subject to significant sanctions, civil and criminal fines and injunctions prohibiting us from engaging in specified promotional conduct. Moreover, our failure to comply with any applicable regulatory requirements could, among other things, result in:

- warning letters;
- fines;
- changes in advertising;
- revocation or suspension of regulatory approvals of products;

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- product recalls or seizures;
- delays, interruption, or suspension of product distribution, marketing and sales;
- civil or criminal sanctions;
- suspension or termination of ongoing clinical trials;
- imposition of restrictions on our operations;
- close the facilities of our CMOs (resulting in our delay or inability to manufacture affected drug products); and
- refusals to approve new products.

The discovery of previously unknown safety risks with drug products approved to go to market may raise costs or prevent us from marketing such products or change the labeling of our products or take other potentially limiting or costly actions if we or others identify safety risks after our products are on the market.

The later discovery of previously unknown safety risks with our products may result in the imposition of restrictions on distribution or use of the drug product, including withdrawal from the market. The FDA may revisit and change its prior determinations with regard to the safety and efficacy of our products. If the FDA's position changes, we may be required to change our labeling or to cease manufacture and marketing of the products at issue. Even prior to any formal regulatory action, we could voluntarily decide to cease the distribution and sale or recall any of our products if concerns about their safety or effectiveness develop.

The FDA has significant authority to take regulatory actions in the event previously unknown safety risks are identified or if data suggest that our products may present a risk to safety. For example, the FDA may:

- require sponsors of marketed products to conduct post-approval clinical studies to assess a known serious risk, signals of serious risk or to identify an unexpected serious risk;
- mandate labeling changes to products, at any point in a product's lifecycle, based on new safety information; and
- require sponsors to implement a REMS for a product which could include a medication guide, patient package insert, a communication plan to healthcare providers, or other elements as the FDA deems are necessary to assure safe use of the drug (either prior to approval or post-approval as necessary).

Failure to comply with a REMS could result in significant civil monetary penalties or other administrative actions by the FDA. Further, regulatory agencies could change existing, or promulgate new, regulations at any time which may affect our ability to obtain or maintain approval of our existing or future products or require significant additional costs to obtain or maintain such approvals.

Legislative or regulatory reform of the healthcare system and pharmaceutical industry related to pricing, coverage or reimbursement may hurt our ability to sell our products profitably or at all.

Our ability to commercialize any products successfully will depend in part on the availability of coverage and reimbursement from third-party payers such as government authorities, private health insurers, health maintenance organizations including pharmacy benefit managers and other health care-related organizations, both in the U.S. and foreign markets. Even if we succeed in bringing one or more products to the market, the amount reimbursed for our products may be insufficient to allow us to compete effectively and could adversely affect our profitability. Coverage and reimbursement by governmental and other third-party payers may depend upon a number of factors, including a governmental or other third-party payer's determination that use of a product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

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Obtaining coverage and reimbursement approval for a product from each third-party and governmental payer is a time-consuming and costly process that could require us to provide supporting scientific, clinical and cost-effectiveness data for the use of our products to each payer. We may not be able to provide data sufficient to obtain coverage and adequate reimbursement.

In both the U.S. and certain foreign jurisdictions, there have been and may continue to be a number of legislative and regulatory proposals related to coverage and reimbursement that could impact our ability to sell our products profitably. The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, collectively referred to as the Healthcare Reform Law, was signed into law on March 30, 2010. The Healthcare Reform Law substantially changed the way healthcare is financed by both governmental and private insurers and significantly impacted the pharmaceutical industry. The Healthcare Reform Law included, among other things, an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, revisions to the definition of "average manufacturer price" for reporting purposes, increases in the amount of rebates owed by drug manufacturers under the Medicaid Drug Rebate Program, expansion of the 340B drug discount program that mandates discounts to certain hospitals, community centers and other qualifying providers, and changes to affect the Medicare Part D coverage gap, or "donut hole." The full effects of these provisions will become apparent as these laws are implemented and the CMS and other agencies issue applicable regulations or guidance as required by the Healthcare Reform Law. Moreover, in the coming years, additional changes could be made to governmental healthcare programs that could significantly impact the success of our products.

The high cost of pharmaceuticals continues to generate substantial government interest. It is possible that proposals will be adopted, or existing regulations that affect the coverage and reimbursement of pharmaceutical and other medical products may change, that may impact our products currently on the market and any of our products approved for marketing in the future. Cost control initiatives could decrease the price that we receive for any of our products or product candidates. In addition, third-party payers are increasingly challenging the price and cost-effectiveness of medical products and services. Significant uncertainty exists as to the coverage and reimbursement status of newly-approved pharmaceutical products. Future developments may require us to decrease the price that we charge for our products, thereby negatively affecting our financial results.

In some foreign countries, particularly in the EU, prescription drug pricing is subject to governmental control. Drug pricing may be made against a reference price set by the healthcare providers as a measure for healthcare cost containment. Pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. If coverage and reimbursement of our products are unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels for the purpose of adoption of these products in the national health services in these jurisdictions, our profitability will likely be negatively affected.

If we market products in a manner that violates health care fraud and abuse laws, we may be subject to civil or criminal penalties, including exclusion from participation in government health care programs.

As a pharmaceutical company, even though we do not provide healthcare services or receive payments directly from or bill directly to Medicare, Medicaid or other third-party payers for our products, certain federal and state healthcare laws and regulations pertaining to fraud and abuse are and will be applicable to our business. We are subject to healthcare fraud and abuse laws by both the federal government and the states in which we conduct our business. The laws that may affect our ability to operate include the federal health care program Anti-Kickback Statute, which prohibits, among other things, knowingly and willfully offering, paying, soliciting, or receiving remuneration to induce or in return for purchasing, leasing, ordering, or arranging for the purchase, lease or order of any health care item or service reimbursable under Medicare, Medicaid or other federally financed health care programs. This statute applies to arrangements between pharmaceutical manufacturers and prescribers, purchasers and formulary managers. Although there are a number of statutory exceptions and regulatory safe harbors protecting certain common activities, the exceptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exception or safe

harbor.

Federal false claims laws prohibit any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to get a false claim paid. Pharmaceutical companies have been prosecuted under these laws for a variety of alleged promotional and marketing activities, such as providing free product to customers with the expectation that the customers would bill federal programs for the product; reporting to pricing services inflated average wholesale prices that were then used by federal programs to set reimbursement rates; engaging in off-label promotion that caused claims to be submitted to Medicaid for non-covered off-label uses; and submitting inflated best price information to the Medicaid Drug Rebate Program.

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The Health Insurance Portability and Accountability Act of 1996 also created prohibitions against health care fraud and false statements relating to health care matters. The health care fraud statute prohibits knowingly and willfully executing a scheme to defraud any health care benefit program, including private payers. The false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for health care benefits, items or services.

In addition, there has been a recent trend of increased federal and state regulation of payments made to physicians. The Healthcare Reform Law imposed new requirements on manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to CMS information related to payments or other "transfers of value" made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, and applicable manufacturers and group purchasing organizations to report annually to CMS ownership and investment interests held by physicians (as defined above) and their immediate family members and payments or other "transfers of value" to such physician owners and their immediate family members. Manufacturers were required to begin data collection on August 1, 2013 and to report such data to the government by March 31, 2014 and by the 90th calendar day of each year thereafter.

The majority of states also have statutes or regulations similar to these federal laws, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payer. In addition, some states have laws that require pharmaceutical companies to adopt comprehensive compliance programs. For example, under California law, pharmaceutical companies must comply with both the April 2003 Office of Inspector General Compliance Program Guidance for Pharmaceutical Manufacturers and the PhRMA Code on Interactions with Healthcare Professionals, as amended. Certain states also mandate the tracking and reporting of gifts, compensation, and other remuneration paid by us to physicians and other health care providers. We have adopted and implemented a compliance program designed to comply with applicable federal, state and local requirements wherever we operate, including but not limited to the laws of the states of California and Nevada.

Although compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Moreover, achieving and sustaining compliance with applicable federal and state laws may prove costly.

Because of the breadth of these laws and the narrowness of the safe harbors, it is possible that some of our business activities could be subject to challenge under one or more of such laws. The Healthcare Reform Law also make several important changes to the federal Anti-Kickback Statute, false claims laws, and health care fraud statute by weakening the intent requirement under the anti-kickback and health care fraud statutes that may make it easier for the government, or whistleblowers to charge such fraud and abuse violations. A person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it. In addition, the Health Care Reform Law provides that the government may assert that a claim including items or services resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim for purposes of the false claims statutes. In addition, the Healthcare Reform Law increases penalties for fraud and abuse violations. If our past, present or future operations are found to be in violation of any of the laws described above or other similar governmental regulations to which we are subject, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and negatively impact our financial results.

We may be subject to product liability claims, and may not have sufficient product liability insurance to cover any such claims, which may expose us to substantial liabilities.

We may be held liable if any product we or our partners develop causes injury or is found otherwise unsuitable during product testing, manufacturing, clinical trials, marketing or sale. Regardless of merit or eventual outcome, product liability claims could result in decreased demand for our product candidates, injury to our reputation, withdrawal of patients from our clinical trials, substantial monetary awards to trial participants and the inability to commercialize any products that we may develop. These claims might be made directly by consumers, health care providers, pharmaceutical companies or others selling or testing our products. Although we currently carry product liability insurance that we believe is adequate, it is possible that this coverage will be insufficient to protect us from future claims. Additionally, our insurance may not reimburse us or may not be sufficient to reimburse us for expenses or losses we may suffer. Moreover, if insurance coverage becomes more expensive, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. Failure to maintain sufficient insurance coverage could have a material adverse effect on our business, prospects and results of operations if claims are made that exceed our coverage.

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On occasion, juries have awarded large judgments in class action lawsuits for claims based on drugs that had unanticipated side effects. In addition, the pharmaceutical and biotechnology industries, in general, have been subject to significant medical malpractice litigation. A successful product liability claim or series of claims brought against us could harm our reputation and business and financial condition.

We could be adversely affected by violations of the U.S. Foreign Corrupt Practices Act, or the FCPA, and other worldwide anti-bribery laws.

We are subject to the FCPA which prohibits companies and their intermediaries from making payments to non-U.S. government officials for purposes of obtaining or retaining business or securing any other improper advantage. We have policies and procedures in place to ensure that we comply with the FCPA and similar laws; however, there is no assurance that such policies and procedures will protect us against liability under the FCPA or related laws for actions taken by our employees and intermediaries with respect to our business. Failure to comply with the FCPA and related laws could disrupt our business and lead to criminal and civil penalties including fines, suspension of our ability to do business with the federal government and denial of government reimbursement of our products, which could result in a material adverse impact on our business, financial condition, results of operations and cash flows. We could also be adversely affected by any allegation that we violated such laws.

The use of hazardous materials, including radioactive and biological materials, in our research and development and commercial efforts imposes certain compliance costs on us and may subject us to liability for claims arising from the use or misuse of these materials.

Our research and development, manufacturing (including a radiolabeling step for ZEVALIN) and administration of our drugs involves the controlled use of hazardous materials, including chemicals, radioactive and biological materials, such as radioactive isotopes. We are subject to federal, state, local and foreign environmental laws and regulations governing, among other matters, the handling, storage, use and disposal of these materials and some waste products. We cannot completely eliminate the risk of contamination or injury from these materials and we could be held liable for any damages that result, which could exceed our financial resources. We currently maintain insurance coverage for injuries resulting from the hazardous materials we use; however, future claims may exceed the amount of our coverage. Also, we do not have insurance coverage for pollution cleanup and removal. Currently the costs of complying with such federal, state, local and foreign environmental regulations are not significant, and consist primarily of waste disposal expenses. However, they could become expensive, and current or future environmental laws or regulations may impair our research, development, production and commercialization efforts.

Risks Related to Our Common Stock

There are a substantial number of shares of our common stock eligible for future sale in the public market. The sale of these shares could cause the market price of our common stock to fall. Any future equity issuances by us may have dilutive and other effects on our existing stockholders.

As of December 31, 2016, there were approximately 80 million shares of our common stock outstanding. Security holders held outstanding options, restricted stock units, warrants, preferred stock and convertible notes which, if vested, exercised or converted, would obligate us to issue up to approximately 25 million additional shares of common stock. A substantial number of those shares, when we issue them upon vesting, conversion or exercise, will be available for immediate resale in the public market. In addition, we have reserved an aggregate of 11 million shares of our common stock for future issuance under our equity compensation plans. We may also sell additional shares of common stock or securities convertible or exercisable into common stock in public or private offerings, which would be available for resale in the market. Certain issuances by us of equity securities may be at or below the prevailing market price of our common stock and may have a dilutive impact on our existing stockholders. These issuances or other dilutive issuances would also cause our net income, if any, per share to decrease in future periods. The market price of our common stock could fall as a result of sales of any of these shares of common stock due to the increased number of shares available for sale in the market.

The convertible note hedge and warrant transactions that we entered into in December 2013 may affect the value of our common stock.

In connection with the pricing of our convertible notes in December 2013, we entered into convertible note hedge transactions and separate warrant transactions with RBC Capital Markets, LLC, or RBC. The convertible note hedge transactions are expected generally to reduce the potential dilution upon any conversion of the notes and/or offset any cash

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payments we are required to make in excess of the principal amount of converted notes, as the case may be. The warrant transactions could separately have a dilutive effect to the extent that the market price per share of our common stock exceeds the strike price of the warrants. RBC and/or its affiliates may modify their hedge positions by entering into or unwinding various derivatives with respect to our common stock and/or purchasing or selling our common stock in secondary market transactions prior to the maturity of the convertible notes (and is likely to do so during any observation period related to a conversion of notes). This activity could cause or avoid an increase or a decrease in the market price of our common stock.

In addition, if the convertible note hedge and warrant transactions fail to become effective, through the failure of counterparties to perform or otherwise, RBC and/or its affiliates may unwind its hedge positions with respect to our common stock, which could adversely affect the value of our common stock. The potential effect, if any, of these transactions and activities on the market price of our common stock will depend in part on market conditions and cannot be ascertained at this time (though could adversely affect the value of our common stock).

We are subject to the risks of securities and related litigation, which may expose us to substantial liabilities and could seriously harm our business.

We may be subject to risk of securities litigation and derivative actions from time to time as a result of being publicly traded, including the remaining unresolved actions set forth in “Item 3. Legal Proceedings.” There can be no assurance that any settlement or liabilities in such actions or any future lawsuits or claims against us would be covered or partially covered by our insurance policies, which could have a material adverse effect on our earnings in one or more periods. While we and our Board of Directors deny the allegations of wrongdoing against us in the unresolved actions initiated against us, there can be no assurance as to the ultimate outcome or timing of their resolutions. In addition to the potential costs and liabilities, securities litigation could divert management’s attention and resources, which could seriously harm our business.

The market price and trading volume of our common stock fluctuate significantly and could result in substantial losses for individual investors.

The stock market from time to time experiences significant price and trading volume fluctuations that are unrelated to the operating performance of particular companies. These broad market fluctuations may cause the market price and trading volume of our common stock to decrease. In addition, the market price and trading volume of our common stock is often highly volatile.

Factors that may cause the market price and volume of our common stock to decrease include, among other things:

- recognition on up-front licensing or other fees or revenues;
- payments of non-refundable up-front or license fees, or payment for cost-sharing expenses, to third parties;
- adverse results or delays in our clinical trials;
- fluctuations in our results of operations;
- timing and announcements of our technological innovations or new products or those of our competitors;
- developments concerning any strategic alliances or acquisitions we may enter into;
- announcements of FDA non-approval of our products, or delays in the FDA or other foreign regulatory review process or actions;
- changes in recommendations or guidelines of government agencies or other third parties regarding the use of our products;
- adverse actions taken by regulatory agencies with respect to our drug products, clinical trials, manufacturing processes or sales and marketing activities;
- concerns about our products being reimbursed;
- any lawsuit involving us or our products;
- developments with respect to our patents and proprietary rights;
- public concern as to the safety of products developed by us or others;
- regulatory developments in the U.S. and in foreign countries;

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- changes in stock market analyst recommendations regarding our common stock or lack of analyst coverage;
- the pharmaceutical industry generally and general market conditions;
- failure of our results of operations to meet the expectations of stock market analysts and investors;
- sales of our common stock by our executive officers, directors and significant stockholders or sales of substantial amounts of our common stock generally;
- hedging or arbitrage transactions by holders of our convertible notes;
- changes in accounting principles; and
- loss of any of our key scientific or management personnel.

Also, certain dilutive securities such as warrants can be used as hedging tools which may increase volatility in our stock and cause a price decline. While a decrease in market price could result in direct economic loss for an individual investor, low trading volume could limit an individual investor's ability to sell our common stock, which could result in substantial economic loss as well. From January 4, 2016 through February 28, 2017, the closing price of our common stock ranged between $3.22 and $7.65, and the daily trading volume was as high as 3.7 million shares and as low as 0.2 million shares.

Following periods of volatility in the market price of a company's securities, a securities class action litigation may be instituted against that company. Regardless of their merit, these types of lawsuits generally result in substantial legal fees and management's attention and resources being diverted from the operations of a business.

Provisions of our charter, bylaws and stockholder rights plan may make it more difficult for someone to acquire control of us or replace current management even if doing so would benefit our stockholders, which may lower the price an acquirer or investor would pay for our stock.

Provisions of our certificate of incorporation and bylaws, both as amended, may make it more difficult for someone to acquire control of us or replace our current management. These provisions include:

- the ability of our board of directors to amend our bylaws without stockholder approval;
- the inability of stockholders to call special meetings;
- the ability of members of the board of directors to fill vacancies on the board of directors;
- the inability of stockholders to act by written consent, unless such consent is unanimous; and
- the establishment of advance notice requirements for nomination for election to our board of directors or for proposing matters that can be acted on by stockholders at stockholder meetings.

These provisions may make it more difficult for stockholders to take certain corporate actions and could delay, discourage or prevent someone from acquiring our business or replacing our current management, even if doing so would benefit our stockholders. These provisions could limit the price that certain investors might be willing to pay for shares of our common stock.

We have a stockholder rights plan pursuant to which we distributed rights to purchase units of our Series B junior participating preferred stock. The rights become exercisable upon the earlier of ten days after a person or group of affiliated or associated persons has acquired 15% or more of the outstanding shares of our common stock or ten business days after a tender offer has commenced that would result in a person or group beneficially owning 15% or more of our outstanding common stock. These rights could delay or discourage someone from acquiring our business, even if doing so would benefit our stockholders. We currently have no stockholders who own 15% or more of the outstanding shares of our common stock.

Our failure to establish and maintain effective internal control over financial reporting could result in material misstatements in our financial statements, our failure to meet our reporting obligations and cause investors to lose confidence in our reported financial information, which in turn could cause the trading price of our common stock to decline.

Maintaining effective internal control over financial reporting is necessary for us to produce reliable financial statements. In connection with our assessment of the effectiveness of internal control over financial reporting and the preparation of our financial statements for the year ended December 31, 2013, we identified a material weakness related to ineffective design and operation of controls over our process of estimating the required period-end accruals

for operating expenses, which resulted in

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net overstated operating expenses and accrued liabilities in multiple reporting periods in, and prior to, 2013. We have remediated this material weakness as of December 31, 2014. Accordingly, material weaknesses have adversely affected us in the past and could affect us in the future.

The results of our periodic management evaluations and annual auditor attestation reports regarding the effectiveness of our internal control over financial reporting are required by the Sarbanes-Oxley Act of 2002. Any failure to maintain enhanced monitoring controls and improved detection and communication of financial misstatements across all levels of the organization could result in (i) additional material weaknesses, (ii) material misstatements in our financial statements, requiring restatements of our previously-filed financial statements, and (iii) cause us to fail to meet our timely reporting and debt compliance obligations. These outcomes could cause us to lose public confidence, and could cause the trading price of our common stock to decline. For further information regarding our controls and procedures, see Item 9A. Controls and Procedures in this Annual Report on Form 10-K.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

We lease 12,000 square feet for our principal executive office in Henderson, Nevada under a non-cancelable operating lease expiring April 30, 2019, and we also lease 56,000 square feet for our administrative and research and development facility in Irvine, California under a non-cancelable operating lease expiring May 31, 2019. We also lease administrative space in Westlake Village, California; Westminster, Colorado; and Mumbai, India. We believe that these leased facilities are adequate to meet our current and planned business needs.

ITEM 3. LEGAL PROCEEDINGS

We are involved from time-to-time with various legal matters arising in the ordinary course of business. These claims and legal proceedings are of a nature we believe are normal and incidental to a pharmaceutical business, and may include product liability, intellectual property, employment matters, and other general claims.

We make provisions for liabilities when it is both probable that a liability has been incurred and the amount of the loss can be reasonably estimated. Such provisions are assessed at least quarterly and adjusted to reflect the impact of any settlement negotiations, judicial and administrative rulings, advice of legal counsel, and other information and events pertaining to a particular case. Litigation is inherently unpredictable. Although the ultimate resolution of these various matters cannot be determined at this time, we do not believe that such matters, individually or in the aggregate, will have a material adverse effect on our consolidated results of operations, cash flows, or financial condition.

ANDA Litigation

On June 3, 2016, the U.S. Court of Appeals for the District of Columbia affirmed judgment in favor of the FDA et. al in an action we brought April 27, 2015 seeking a temporary restraining order or preliminary injunction to suspend FDA approval of Sandoz’s ANDA of FUSILEV. On June 9, 2016 and June 22, 2016, respectively, judgment was entered in favor of additional parties who had filed separate ANDAs to manufacture generic versions of FUSILEV.

On June 19, 2014, we filed a lawsuit against five parties resulting from Paragraph IV certifications in connection with four separate ANDAs to manufacture a generic version of FOLOTYN. We reached confidential settlement agreements with each defendant and the FOLOTYN litigation has been dismissed as of August 17, 2016. As a result of the settlements, the defendants will be permitted to market a generic version of FOLOTYN in the United States commencing on November 15, 2022 or earlier under certain circumstances. All costs pertaining to these matters (incurred and accrued) have been recognized within "selling, general and administrative" expenses on the accompanying Consolidated Statements of Operations for all periods presented.

Stockholder Litigation

John Perry v. Spectrum Pharmaceuticals, Inc. et al. (Filed March 14, 2013 in United States District Court, District of Nevada; Case Number 2:2013-cv-00433-LDG-CWH). This consolidated class action raises substantially identical claims and allegations against defendants Spectrum Pharmaceuticals, Inc., Dr. Rajesh C. Shrotriya, Brett L. Scott, and Joseph Kenneth

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Keller. The alleged class period is August 8, 2012 to March 12, 2013. The lawsuits allege a violation of Section 10(b) of the Securities Exchange Act of 1934 against all defendants and control person liability, as a violation of Section 20(b) of the Securities Exchange Act of 1934, against the individual defendants. The claims purportedly stem from our March 12, 2013 press release, which announced an anticipated change in ordering patterns of FUSILEV. On October 27, 2015, we reached a $7 million settlement in principle with the lead plaintiff (which involved our insurance carrier, as the reimbursing party in full). On June 13, 2016, the Court entered an order granting final approval of the settlement, a portion of which has been paid as of December 31, 2016, while the remainder is subject to the on-going claims administrative process.

Timothy Fik v. Rajesh C. Shrotriya, et al. (Filed April 11, 2013 in United States District Court, District of Nevada; Case Number 2:2013-cv-00624-JCM-CWH); Christopher J. Watkins v. Rajesh C. Shrotriya, et al. (Filed April 22, 2013 in United States District Court, District of Nevada; Case Number 2:2013-cv-00684-JCM-VCF); and Stefan Muenchhagen v. Rajesh C. Shrotriya, et al. (Filed May 28, 2013; Case Number 2:2013-cv-00942-APG-PAL). These consolidated federal derivative actions are brought by the respective purported stockholders on behalf of nominal plaintiff Spectrum against certain current and former directors and officers. The complaints generally allege breaches of fiduciary duty based on conduct relating to a March 12, 2013 press release concerning sales of Spectrum's product FUSILEV. The complaints seek compensatory damages, corporate governance reforms, restitution and disgorgement of defendants' alleged profits, and costs and fees. These actions are stayed. Settlement discussions are ongoing, and accordingly, no agreement has yet been reached to resolve these derivative complaints. If a settlement were reached, we believe it would be reimbursable by our insurance carrier, and would be subject to preliminary and final court approval. We have estimated and accrued for this settlement within "selling, general and administrative expenses" in our accompanying Consolidated Statements of Operations for the year ended December 31, 2016, and within "other accrued liabilities" in our accompanying Consolidated Balance Sheets as of December 31, 2016.

Hardik Kakadia v. Rajesh C. Shrotriya, et al. (Filed April 23, 2013 in the Eighth Judicial District Court of the State of Nevada in and for Clark County; Case Number A-13-680643-B); and Joel Besner v. Rajesh C. Shrotriya, et al. (Filed May 31, 2013; Case Number A-13-682668-C) (collectively the "State Derivative Actions"). These consolidated state derivative actions are brought by the respective purported stockholders on behalf of nominal plaintiff Spectrum against certain current and former directors and officers and are substantially similar to the consolidated federal derivative actions (described in the paragraph above). These actions are stayed. Settlement discussions are ongoing, and accordingly, no agreement has yet been reached to resolve these derivative complaints. If a settlement were reached, we believe it would be reimbursable by our insurance carrier, and would be subject to preliminary and final court approval. We have estimated and accrued for this settlement within "selling, general and administrative expenses" in our accompanying Consolidated Statements of Operations for the year ended December 31, 2016, and within "other accrued liabilities" in our accompanying Consolidated Balance Sheets as of December 31, 2016.

Olutayo Ayeni v. Spectrum Pharmaceuticals, Inc., et al. (Filed September 21, 2016 in the United States District Court, Central District of California; Case No. 2:16-cv-07074) (the "Ayeni Action") and Glen Hartsock v. Spectrum Pharmaceuticals, Inc., et al. (Filed September 28, 2016 in the United States District Court, District Court of Nevada Case; No. 2:16-cv-02279-RFB-GWF) (the "Hartsock Action"). On November 15, 2016, the Ayeni Action was transferred to the United States District Court, District Court of Nevada. The parties have stipulated to the consolidation of the Ayeni Action with the Hartsock Action. These class action lawsuits allege that we and certain of our executive officers made false or misleading statements and failed to disclose material facts about our business and the prospects of approval for our NDA to the FDA for QAPZOLA in violation of Section 10(b) (and Rule 10b-5 promulgated thereunder) and 20(a) of the Securities Exchange Act of 1934, as amended. The plaintiffs seek damages, interest, costs, attorneys' fees, and other unspecified equitable relief. We believe that these claims are without merit, and intend to vigorously defend against these claims. The value of a potential settlement cannot be reasonably estimated given its highly uncertain nature as of December 31, 2016.

Wells v. Rajesh C. Shrotriya, et al. (Filed February 23, 2017, in the United States District Court for the District of Delaware; Case No. 1:17-cv-00191-UNA). A shareholder filed a derivative complaint purportedly on behalf of

nominal plaintiff Spectrum against certain current and former directors and executive officers. The complaint is related to the same underlying factual allegations as the Ayeni Action and the Hartsock Action described above, and generally alleges claims for breaches of fiduciary duties, unjust enrichment, abuse of control, gross mismanagement, waste of corporate assets, and violations of Section 14(A) of the Securities Exchange Act of 1934. The plaintiff seeks declaratory relief and damages. We believe that these claims are without merit, and intend to vigorously defend against these claims. The value of a potential settlement cannot be reasonably estimated given its highly uncertain nature as of December 31, 2016.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

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PART II.

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Our common stock is traded on the NASDAQ Global Select Market under the symbol "SPPI." The high and low closing sale prices of our common stock as reported by NASDAQ during each quarter ended in fiscal years 2016 and 2015 were as follows:

	High	Low
Year Ended December 31, 2016:		
First Quarter	$6.36	$4.28
Second Quarter	7.65	6.33
Third Quarter	7.10	4.47
Fourth Quarter	4.79	3.22
Year Ended December 31, 2015:		
First Quarter	$7.66	$5.95
Second Quarter	7.37	5.65
Third Quarter	7.60	5.92
Fourth Quarter	6.93	5.07

On February 28, 2017, the closing price of our common stock on the NASDAQ Global Select Market was $6.40 per share, and there were 411 holders of record of our common stock.

During the year ended December 31, 2016, we purchased an aggregate of 266,860 shares of common stock surrendered by our employees and members of our board of directors to satisfy their income tax withholding obligations of their restricted stock awards at an average price of $5.32 per share. Such shares have been canceled by our transfer agent. The following table provides information regarding our repurchases for the twelve months ended December 31, 2016.

Period	Total Number of Shares Purchased	Average Price Paid Per Share	Total Number of Shares Purchased as Part of Publicly Announced Plans or Programs	Maximum Number of Shares (or Approximate Dollar Value) that May Yet Be Purchased Under the Plans or Programs
January 1, 2016 - December 31, 2016	266,860	$ 5.32	—	$ —

Stock Performance Graph (1)

The graph below compares the cumulative total stockholder return on $100 invested, assuming the reinvestment of all dividends, on December 31, 2011, the last trading day before our 2011 fiscal year, through the end of fiscal 2016 with the cumulative total return on $100 invested for the same period in the Russell 2000 index, our New Peer Group and our Old Peer Group.

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The New Peer Group (which we believe more closely reflects our operations and business characteristics than the Old Peer Group) was identified by selecting a comparably sized, industry-affiliated peer group of companies operating within the biotechnology or pharmaceutical industries, with 2015 revenues of between $60 million and $500 million with market capitalization of up to approximately $1.0 billion. In the prior year, the Old Peer Group had market capitalization of up to approximately $1.5 billion.

Our New Peer Group consists of the following publicly-traded companies:

- AMAG Pharmaceuticals, Inc.
- Albany Molecular Research Inc.
- Affymetrix, Inc.
- Genomic Health, Inc.
- Luminex Corporation
- Amphastar Pharmaceuticals, Inc.
- MiMedx Group, Inc.
- Pernix Therapeutics Holdings, Inc.
- SciClone Pharmaceuticals, Inc.
- Supernus Pharmaceuticals, Inc.

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- Halozyme Therapeutics, Inc.
- Sucampo Pharmaceuticals, Inc.
- Enanta Pharmaceuticals, Inc.
- Sequenom Inc.
- Fluidigm Corporation
- Harvard Bioscience, Inc.
- Vanda Pharmaceuticals Inc.
- Infinity Pharmaceuticals, Inc.
- VIVUS, Inc.
- Merrimack Pharmaceuticals, Inc.
- NewLink Genetics Corporation
- Eagle Pharmaceuticals, Inc.

Our Old Peer Group consisted of the following publicly-traded companies:

- Acorda Therapeutics, Inc.
- Aegerion Pharmaceuticals, Inc.
- Auxilium Pharmaceuticals, Inc.
- Dendreon Corp.
- DepoMed Inc.
- Emergent BioSolutions, Inc.
- Genomic Health Inc.
- Hyperion Therapeutics, Inc.
- INSYS Therapeutics, Inc.
- Sagent Pharmaceuticals, Inc.
- SciClone Pharmaceuticals, Inc.
- Sucampo Pharmaceuticals, Inc.
- Supernus Pharmaceuticals, Inc.
- The Medicines Company
- VIVUS Inc.

	12/31/2011	12/31/2012	12/31/2013	12/31/2014	12/31/2015	12/31/2016
Spectrum Pharmaceuticals, Inc.	$ 100	$ 77	$ 61	$ 48	$ 42	$ 31
Russell 2000	$ 100	$ 116	$ 162	$ 169	$ 162	$ 196
Old Peer Group	$ 100	$ 116	$ 141	$ 152	$ 185	$ 147
New Peer Group	$ 100	$ 126	$ 123	$ 143	$ 139	$ 131

(1) The information in this section is not “soliciting material,” is not deemed “filed” with the SEC and is not to be incorporated by reference in any filing of the Company under the Securities Act or the Exchange Act, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing.

Dividend Policy

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We have not paid dividends on our common stock during the most two recent fiscal years. We currently intend to retain all earnings, if any, for use in the expansion of our business and do not anticipate paying any dividends in the foreseeable future. However, the payment of dividends, if any, will be at the discretion of the Board of Directors and subject to compliance at such time with any applicable restrictions contained in our various agreements.

ITEM 6. SELECTED FINANCIAL DATA

The following selected consolidated financial data has been derived from our audited Consolidated Financial Statements. The audited Consolidated Financial Statements for the fiscal years ended December 31, 2016, 2015, and 2014 are included elsewhere in this Annual Report on Form 10-K. The information set forth below should be read in conjunction with Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations and the Consolidated Financial Statements and Notes thereto in Item 8. Financial Statements and Supplementary Data. The information set forth below is not necessarily indicative of our future financial condition or results of operations.

	Year ended December 31,				
Selected Statement of Operations Data:	2016	2015	2014	2013	2012
	(In thousands, except per share data)				
Total revenues	$146,444	$162,556	$186,830	$155,854	$267,707
Operating costs and expenses:					
Cost of product sales (excludes amortization and impairment of intangible assets)	27,953	27,689	27,037	28,580	46,633
Cost of service revenue	7,890	—	—	—	—
Selling, general and administrative	87,347	86,514	97,412	99,315	89,922
Research and development	58,936	50,766	69,662	46,670	41,560
Amortization and impairment of intangible assets	25,946	38,319	24,288	20,074	8,818
(Loss) Income from operations	(61,628)	(40,732)	(31,569)	(38,785)	80,774
Change in fair value of contingent consideration related to acquisitions	(649)	676	987	2,871	—
Other (expense), net	(8,548)	(10,323)	(12,951)	(722)	(844)
(Loss) income before provision for income taxes	(70,825)	(50,379)	(43,533)	(36,636)	79,930
Benefit (provision) for income taxes	2,313	(406)	(2,186)	(25,498)	14,271
Net (loss) income	$(68,512)	$(50,785)	$(45,719)	$(62,134)	$94,201
Net (loss) income per share—basic	$(0.94)	$(0.78)	$(0.71)	$(1.02)	$1.61
Net (loss) income per share—diluted	$(0.94)	$(0.78)	$(0.71)	$(1.02)	$1.46

	As of December 31,				
Selected Balance Sheet Data:	2016	2015	2014	2013	2012
	(In thousands)				
Working capital surplus (current assets minus current liabilities)	$151,137	$114,282	$113,030	$145,206	$141,630
Total assets	$428,768	$419,049	$490,033	$499,155	$504,955
Long term obligations, less current portion	$127,229	$129,849	$126,040	$127,565	$93,031
Total stockholders' equity					